

LIVING KIDNEY DONOR FOLLOW-UP IN A STATEWIDE HEALTH  
INFORMATION EXCHANGE: HEALTH SERVICES UTILIZATION, HEALTH  
OUTCOMES AND POLICY IMPLICATIONS

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## DEDICATION

This dissertation is dedicated to my cousin Marc Thompson and the rest of my family, who taught me how to live a life full of gratitude and who encouraged me to seek a career in service to the field of organ donation and transplantation.



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## PREFACE

The purpose of this dissertation is to introduce and to demonstrate a new approach to supporting the follow-up care of living kidney donors. This new methodology, an exploratory process utilizing the tools of clinical informatics applied in a statewide health information exchange, can be used to identify, capture, and to then assess health outcomes of living kidney donors in the 24-month or two-year follow-up period currently that is required by United Network for Organ Sharing policy.

This dissertation should be of interest to high-level decision makers, in the Scientific Registry of Transplant Recipients and the Organ Procurement and Transplantation network specifically, but also in other large private and public organizations. It should also be of interest to scholars of applied clinical informatics, transplant administration, and surgery departments with living donor kidney transplant programs.

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Living donors have contributed about 6,000 kidneys per year in the past 10 years, but more than 100,000 individuals are still waiting for a kidney transplant. Living kidney donors undergo a major surgical procedure without direct medical benefit to themselves, but comprehensive follow-up information on living donors' health is unfortunately limited. Expert recommendations suggest capturing clinical information beyond traditional sources to improve surveillance of co-morbid conditions from living kidney donors. Currently the United Network for Organ Sharing is responsible for collecting and reporting follow-up data for all living donors from U.S. transplant centers. Under policy implemented in February of 2013, transplant centers must submit follow-up data for two years after donation, but current processes often yield to incomplete and untimely reporting. This dissertation uses a statewide Health Information Exchange as a new clinical data source to 1) retrospectively identify a cohort of living kidney donors, 2) understand their follow-up care patterns, and 3) observe selected clinical outcomes including hypertension, diabetes and post-donation renal function.

Cynthia Stone, DrPH, Chair

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## LIST OF ABBREVIATIONS

ACR, albumin/creatinine ratio

AHRQ, Agency for Healthcare Research and Quality

CKD, chronic kidney disease

CPT, Current Procedural Terminology

DM, diabetes mellitus

eGFR, estimated glomerular filtration rate

EHR, electronic health record

ESRD, end-stage renal disease

HIE, Health Information Exchange

HITECH Act, Health Information Technology for Economic and Clinical Health Act

HRSA, Health Resources and Services Administration

HTN, hypertension

ICD-9-CM, International Classification of Diseases Ninth Edition Clinical Modification

INPC, Indiana Network for Patient Care

KDIGO, Kidney Disease Improving Global Outcomes

LKD; living kidney donors

NLP, natural language processing

OPTN, Organ Procurement and Transplantation Network

SCr, serum creatinine

SRTR, Scientific Registry of Transplant Recipients

UA, urinalysis

UNOS, United Network for Organ Sharing

USRDS, United States Renal Data System

## CHAPTER ONE: INTRODUCTION

### Overview and History of the Current U.S. System of Organ Donation

The first successful kidney transplant took place in 1954 between twin brothers, paving the way for the development of the U.S. system for organ donation, recovery, allocation, and transplantation (Merrill, Murray, Harrison, & Guild, 1956). Since then, the growth and development of the field of transplantation including its structure have been guided by state and federal laws and regulations, making the organ transplant system one of the most complexly regulated areas of healthcare.

### *The Organ Procurement and Transplantation Network*

The Organ Procurement and Transplantation Network (OPTN) was created by the enactment of the National Organ Transplant Act ("National Organ Transplant Act," 1984). The OPTN is charged with developing policies for and implementing an equitable system of organ allocation, maintaining the waiting list of potential organ recipients and collecting and compiling data from all transplant centers in the U.S. All of the 58 federally designated organ procurement organizations (OPOs) serving geographically defined donor service areas and transplant centers are required to participate in the OPTN.

### *The United Network for Organ Sharing*

The United Network for Organ Sharing (UNOS) is a non-profit, private and voluntary organization that has been the sole administrator of the OPTN since the initial contract was awarded in 1986. In other words, UNOS is the substantive body of the OPTN. The Division of Transplantation in the Health Resources and Services

Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) is the governmental agency responsible for the oversight of the OPTN contract.

### Laws, Regulation and Legislation in Organ Transplantation

There are four main types of regulations in organ transplantation, including state laws, federal laws, federal regulations and United Network for Organ Sharing policies. The relevant legislation for organ donation and transplantation is listed in Table 1.1. In general, laws at the state level cover issues relating to the donation process including authorization, scope of public education programs, composition of deceased donor registries, and criteria for the determination of death.

Federal laws on organ transplantation are primarily found in Title 42 of the United States Code ‘The Public Health and Welfare.’ Federal law relating to organ transplantation has a broad approach, primarily outlining the process of organ procurement and allocation by the OPTN. Of prime importance in Title 42 U.S.C. is Section 274a, which establishes the Scientific Registry of Transplant Recipients (SRTR). In addition, 42 U.S.C. Sec. 274e sets limitations and boundaries on the transfer of organs from one person to another, including the prohibition on buying and selling organs.

Also important within federal law (42 U.S.C. 217a; Section 222 of the Public Health Service Act, as amended 42 CFR 121.12) is the establishment of the Advisory Committee on Organ Transplantation (ACOT). This advisory committee was established to assist the HHS Secretary in enhancing organ donation, ensuring that the system of organ transplantation is grounded in the best available medical science, assuring the public that the system is as effective and equitable as possible, and increasing public confidence in the integrity and effectiveness of the transplantation system. HRSA’s

Healthcare Systems Bureau provides ACOT's management and administrative support services and records are to be made available for public inspection and copying ("Freedom of Information Act," 1967). In contrast, federal legislation expands federal law and provides provisions for how transplant centers; OPOs and the OPTN should function. Federal regulations explain internal structures of organizations and their primary operations.

UNOS rules are policies that every transplant center and OPO must follow in order to be a member of the OPTN. UNOS policies are developed through an administrative process that is transparent with the public. Specific committees, comprised of members appointed and approved by the president of the OPTN, develop policy proposals and disseminate them justifying their need. Next, the UNOS committee asks for public comments on policy proposals, where all interested parties are encouraged to submit responses to the proposed policy. After the public comment period concludes, the UNOS committee responds to public comments and submits a final proposal to the Board of Directors for their vote. Should the Board of Directors approve the proposal, the policy then becomes UNOS/OPTN rule. Policies approved by the Board of Directors with or without amendments are implemented according to the OPTN Bylaws Article XI. Policies approved by the Board of Directors and recommended to be enforced as mandatory policies are forwarded for the Secretary of HHS for review and comment 60 days before implementation (OPTN Final Rule, section 121.4(b) (2)).



**Table 1.1- History of Legislation in the U.S. Organ Transplant System**

1968	Uniform Anatomical Gift Act (UAGA)  *Model state law	Provided a uniform legal environment for organ donation; adopted by all 50 states and D.C.; gives all adults the right to donate their bodies or organs for use upon their death “without subsequent veto” by others
1981	Uniform Determination of Death Act (UDAA)  *Model state law	Codified and extended existing common law basis for the determination of death  States that, “An individual who has sustained either irreversible cessation of circulatory and respiratory functions, or irreversible cessation of all functions of the entire brain, including the brain stem, is ‘dead’
1984	National Organ Transplant Act (NOTA) Public Law 98-507	Established the Organ Procurement and Transplantation Network (OPTN) to be run by a non-profit entity → United Network for Organ Sharing (UNOS). Provided grants to expand regional organ procurement organizations, prohibited commercial transactions in organs, and established a Task Force on Organ Transplantation
1986	Omnibus Budget Reconciliation Act (OBRA) Public Law 100-203	Required that hospitals participating in Centers for Medicare and Medicaid Services (Medicare/Medicaid) implement a ‘required request’ policy mandating education about organ donation upon eligible deaths
1987	Amended UAGA	Enacted in 25 jurisdictions; explicitly provides first person-consent honoring donor autonomy, prohibited sale of body organs, and included required request provisions
2004	Organ Donation and Recovery and Improvement Act (ODRIA) Public Law 108-216	Authorized provision of grants for reimbursement for travel, food and other expenses incurred by living donors; established a public education program aimed at increasing awareness for organ donation; authorized grants for study, demonstration projects and outreach activities designed to increase rates of organ donation
2007	Charlie W. Norwood Living Organ Donation Act Public Law 110-144	Amended NOTA to reflect incompatible paired kidney exchange in transplantation as a practice that *does not* constitute ‘valuable consideration’
2013	HIV Organ Policy Equity (HOPE) Act Public Law 113-51	Modifies rules regarding organ donation between HIV-positive individuals; requires OPTN to adopt new standards (including quality) and testing with respect to organs infected with human immunodeficiency virus; directs Secretary of Health and Human Services to publish research guidelines with respect to transplantation of HIV-infected donors and to annually review this scientific research; amends the federal criminal code against HIV-positive individuals who give organs

## Kidney Disease and Transplantation in the United States

Kidney disease statistics for the United States convey the burden of chronic kidney disease (CKD) and end-stage renal disease (ESRD) for which kidney transplantation is the preferred treatment (Coresh, Astor, Greene, Eknoyan, & Levey, 2003; Coresh et al., 2007; A. S. Levey & Coresh, 2012; A. S. Levey et al., 2003). The Centers for Disease Control and Prevention (CDC) estimate one in ten American adults, more than 20 million, have some level of CKD. Data from the U.S. Renal Data Service (USRDS) showed at the end of 2009, more than 871,000 people were being treated for ESRD in the U.S. Historically, between 1980 and 2009, the prevalence rate for ESRD increased nearly 600%, from 290 to 1,738 cases per million. According to the National Institute of Diabetes and Digestive and Kidney Diseases, diabetes and high blood pressure (hypertension) are the most common causes of kidney failure, but other factors include heart and blood vessel disease, and a family history of kidney failure. African-Americans, Hispanics/Latinos, and American Indians are more likely to have kidney failure (USRDS, 2010). Since 1972, Medicare has covered Americans with CKD and transplantation as a treatment for ESRD through the End Stage Renal Disease Program (Public Law 92-603).

Over 100,000 patients on the national wait list need a kidney transplant and the number of patients awaiting kidney transplantation in the United States has steadily increased over time. The gap between organ supply and demand continues to widen despite initiatives to expand use of nonstandard deceased-donor organs (Metzger et al., 2003; Stratta et al., 2004; Woodside et al., 2012). While increased use of organs from living donors is one strategy to address the need for transplants, rates of live kidney

donation have not increased over the past decade. Data from OPTN shows that living kidney donation rate has in fact declined 17 percent from 2004 to 2014 (Matas et al., 2015). The trend in decreasing living kidney donation has been shown among related donors, while participation in kidney paired donation (exchanges for incompatible pairs) and non-directed (e.g. unrelated) donation have increased since the National Organ Transplant Act was amended in 2007 allowing for these practices ("Charlie W. Norwood Living Organ Donation Act," 2007; Matas et al., 2015).

As a small population within the healthcare system, living donors have contributed about 6,000 kidneys per year in the past 10 years but have made a significant impact. Living donor kidney transplants have better graft survival rates than transplants with deceased donor kidneys, significantly reduce the national waiting list, allow for incompatible kidney paired donation, and permit for preemptive renal transplantation prior to dialysis for ESRD (Matas et al., 2015; Waterman et al., 2015).

#### Living Kidney Donor Follow-Up Policy

The routine collection of short-term follow-up data on living donor outcomes is increasingly common. While to date most efforts focus on living donor clinical and laboratory data, psychosocial parameters, such as if the donor has returned to work, are also collected in the U.S. (OPTN, 2016b). In February 2013, the OPTN implemented policy requirements on living donor follow-up for all transplant centers in the United States. This was done in order to promote consistency in the informed consent process, medical and psychosocial evaluation, and medical follow-up received by living donors (OPTN, 2013). In 2014, OPTN requirements were incorporated within national health policies for living donors including liver and kidney-specific requirements. These health

policies created and approved by the OPTN/UNOS Living Donor Committee and subsequently the OPTN Board of Directors define minimum follow-up requirements (OPTN, 2016d), which can and should be expanded upon within center-specific protocols based on local experience and on a case-by-case basis.

The data regarding short-term complications following donor nephrectomy are reliable according to reports from North and South America, Europe, and Asia (Lentine & Patel, 2012). Currently all OPTN/UNOS member transplant centers must submit living donor data at hospital discharge within 6 weeks after donation, whichever is earlier, as well as at 6 months, 1 year, and 2 years after donation. The submission of donor follow-up information is required by OPTN through the two years post-donation, but the level of missing data in submitted forms does not improve their value (M. Dew et al., 2011; Ommen, LaPointe Rudow, Medapalli, Schröppel, & Murphy, 2011).

Living donors with missing data on follow-up forms are more likely to have characteristics that increase their risk for future medical problems, including the development of hypertension and diabetes. In a survey of U.S. transplant programs, approximately 40% of lost contact with more than 75% of their donors by 2 years after donation (Waterman et al., 2013). In the same study, when asked about how long a donor's health should be monitored post-donation, 31% of living kidney donor transplant program respondents endorsed 5 years or more, 30% endorsed 2 years, 32% endorsed 1 year, and 8% endorsed 6 months or less. With the modifications to UNOS/OPTN policies implemented in 2013, all transplant centers with living donor programs must submit forms complete (i.e. without any missing information) for the majority of kidney donors (OPTN, 2016a).

The rationale for required follow-up for living kidney donors is at the foundation of the transplant system's ethical obligation to ensure donor safety as well as the affirmative duty to provide ongoing data surveillance to inform future donors on the risks and benefits including long-term outcomes of donation. Comprehensive follow-up information of living donors' health is limited. Recently a consensus conference on the follow-up care of living kidney donors suggested that specific registries or long-term research efforts should be devoted to the collection of a full range of living donor outcomes including psychosocial and financial outcomes and their relationships with—or increased risk due to—other medical outcomes (M. A. Dew & Jacobs, 2012). In addition, recommendations from the 2010 Living Kidney Donor Follow-Up Conference Writing Group included the need to capture information from sources beyond OPTN and linked data in order to improve the surveillance of comorbid conditions (Leichtman et al., 2011).

#### Preventive and Primary Health Care Services for Living Kidney Donors

New-onset morbidity takes years to emerge, making it unlikely that the 24-month or two-year short-term follow-up currently mandated by OPTN, UNOS, and the Centers for Medicare and Medicaid Services (CMS) provides a comprehensive preventive and primary health approach for living kidney donors. Data shows a minority of donors progressing to CKD, with some even requiring dialysis (Janki et al., 2015; Nazarian & Reese, 2015; Ross, 2015). New data suggests that when living kidney donor renal function declines, the decline occurs more than 5 to 7 years after the donation (Muzaale et al., 2014).

Therefore, with only minimal short-term assessment required by current health policies, living donors may go a long time without any preventive and primary healthcare services. Preventive and primary healthcare services are the favored environment for the management of corrective and preventative clinical measures for the living kidney donor. As with all CKD patients, regular and routine monitoring and laboratory testing can be viewed as an intervention that can delay or stop renal function decline with simple lifestyle modifications (Hallan et al., 2006).

While OPTN/UNOS informed consent policy requires living donors are educated by the transplant center about the need for lifelong annual post-donation physical exams in primary care, two recent cross-sectional follow-up studies suggest that living donors are not engaging in the recommended preventative healthcare activities (OPTN, 2016c). A study of 103 African- American donors from two centers at an average of 6 years post donation showed that 41% were hypertensive; of these, over half (52%) were not receiving treatment and another 17% had inadequately controlled hypertension on medication (Doshi, Goggins, Li, & Garg, 2013). A 2012 study assessed 85 living kidney donors who averaged two years post donation at the time of the study for rates and correlates of health maintenance behaviors; among those studied, 68 living kidney donors had at least one regular medical checkup per year after donation (Myaskovsky et al., 2012). Within this cohort, among the 68 living kidney donors who had post-donation check-ups, 6% reported that their blood pressure was not checked, 26% were not tested for diabetes or high blood glucose levels, and 35% reported not having their urine checked (Myaskovsky et al., 2012). Findings from these studies require verification that

could be accomplished with larger cohorts studied prospectively to improve our understanding of long-term living donor health monitoring and maintenance.

### Big Data and Living Kidney Donors

Few studies have utilized big data sources external to the OPTN/UNOS and linkages with the Scientific Registry of Transplant Recipients (SRTR) to capture living kidney donor health data longitudinally. State Inpatient Databases (SID) provided by the Agency for Healthcare Research and Quality (AHRQ) that includes hospitalizations as well as standard diagnoses and procedure codes occurring during a hospitalization have been used to study living kidney donors (Schold et al., 2014). Schold et al. (2014) explored hospitalizations post-donation and compared them to other abdominal surgical procedures using data from patients in North Carolina, New York, Florida, and California. A limitation of a SID is the inability to track patients across different states limiting the study population to those patients who donated a kidney in the same state as their primary residence. This minimizes the possibility the SID would capture a hospitalization in multiple states. Furthermore this study using AHRQ SID data appeared to have high external validity for identifying living donors given the similarity to national data over the same time period (Schold et al., 2014).

Linked OPTN and administrative private insurer data has been used to study health utilization and pharmacy claims of living kidney donors post-donation in order to assess anti-hypertension medication use (Lentine et al., 2014). While linked pharmacy and external payer data is novel, it is also beyond the scope of standard available transplantation datasets. Limitations of using linked claims data include factors related to

the sample and outcome measures which were derived from insurance data; uninsured living donors are also not captured by this data source.

The presented study will introduce a new source of data that has the potential to improve the frequency and quantity of living kidney donor follow-up. Adapted from a previous descriptive study of sources of ‘big data’ in organ transplantation (Massie, Kuricka, & Segev, 2014), Table 1.2 illustrates a summary of sources available for research in transplantation. This adapted table includes the addition of a new clinical data source, Health Information Exchange (HIE).

**Table 1.2- Summary of Sources Available for Research in Transplantation**

Data Source	Population Included	Strengths	Limitations	Cost
UNOS	Transplant candidates and recipients; living and deceased living donors	Linked to social security death master file; representative of total U.S. transplant population; longitudinal follow-up for transplant recipients	Lacks comorbidities and longitudinal living donor data; does not ascertain kidney graft loss well	Free
SRTR	Living and deceased donors; transplant candidates; transplant recipients	Representative of total U.S. transplant population; longitudinal follow up for transplant recipients; ability to ascertain statistics on graft failure; supplements OPTN data with various secondary sources; ascertains kidney graft loss	Does not contain robust longitudinal living donor data	Standard analysis files (SAFs) available to researchers by request for fee
USRDS	All U.S. patients with ESRD requiring dialysis or kidney transplant since 1995.	Patient data regardless of access to transplantation; rich claims data; provides ESRD incidence for the entire U.S. population; longitudinal follow-up for transplant recipients	Limited claims data (Medicare patients only)	SAFs available to researchers with approved project proposals (for a fee)



AHRQ (National Inpatient Sample)	Inpatients at 20% sample of U.S. hospitals	Patient demographics, ICD- 9-CM diagnoses and procedures; hospital charges; length of stay; discharge disposition; anonymized physician and hospital identifiers; hospital characteristics, rich in data unavailable in OPTN	Created with a stratifying sampling mechanism (not necessarily an unbiased sample of transplant centers and transplant patients); lack of longitudinal information and limited to short-term hospitalization data; cannot be linked to OPTN data as identifiers cannot be released	Available for purchase from AHRQ
AHRQ (State Inpatient Database)	Inpatients at hospitals in 47 U.S. states and the District of Columbia	Over 100 clinical and nonclinical variables included in a hospital discharge abstract	Sample drawn from NIS; expensive and logistically complex for national studies	Costs vary by State and data year
External linkages	Variable depending on external linked dataset (i.e. Pharmacy or private payer claims)	Immunosuppression and other transplant related medication	Challenging to link the data	Costs vary
University Health Consortium	120 academic medical centers and 290 affiliated hospitals in the U.S.	Advantages for use in academic medical centers; focus on quality improvement activities	No specific imperative to collect transplantation data	Available to member institution s
HIE*	Variable based on the Participating institutions and providers	Integrated, longitudinal data across participating providers extracted from electronic health records for large populations	Varies per state	Costs to providers to submit and access data; variable cost to researcher s to access data

\*UNOS = United Network for Organ Sharing; SRTR= Scientific Registry of Transplant Recipients; USRDS = United States Renal Data Service; AHRQ= Agency for Healthcare Research and Quality; HIE =Health Information Exchange  
Table adapted from Massie, A. B., Kuricka, L. M., & Segev, D. L. (2014). Big data in organ transplantation: registries

and administrative claims. *American Journal of Transplantation*, 14(8), 1723-1730.

### Federal Incentives for Use of Health Information Exchange

The enactment of the Health Information Technology for Economic and Clinical Health (HITECH) Act as part of the American Recovery and Reinvestment Act of 2009 improved the adoption and use of electronic health records (EHRs) in the U.S. Thus, early on in the Obama Administration, the U.S. began to prioritize a focus on transforming healthcare delivery into a learning healthcare system that is patient-centered and value-based with supporting technical infrastructures (Aisner, 2007; Friedman, Wong, & Blumenthal, 2010).

The Centers for Medicare & Medicaid Services already has a large role in encouraging HIE through existing Medicare and Medicaid programs and initiatives, as well as new programs authorized under the Affordable Care Act ("Patient Protection and Affordable Care Act, 42 U.S.C.," 2010). A timely interoperable health information exchange (HIE) at the state level is critical to the transformation of the U.S. healthcare system among a variety of healthcare stakeholders (clinicians, laboratories, hospital, pharmacy, health plans, payers and patients) (Brailer, 2005).

According to the Healthcare Information and Management Systems Society, "Interoperability describes the extent to which systems and devices can exchange data, and interpret that shared data" (B. E. Dixon, 2016). Simply put, for two systems to be interoperable, they must be able to exchange data and subsequently present that data such that a user can understand it. EHR interoperability enables better workflow and reduced ambiguity, and allows data transfer among EHR systems and healthcare stakeholders.

Thus, EHRs can ultimately improve the delivery of healthcare by making the right data available at the right time to the right people.

As it is expected that the requirements for living donor reporting will become more rigorous in the future, an exploration into the feasibility of using existing infrastructures such as HIE is timely (Keshvani et al., 2015).

### *Health Information Exchange and the Indiana Network for Patient Care*

Interoperable EHRs are the foundational clinical data exchange to improve patient care. Health information exchange (HIE) is the general term which conveys how clinical information is shared across all providers of healthcare to support care delivery and encompasses strategies and technologies that can facilitate and enable coordinated and connected care across settings, which can improve health, healthcare delivery and cost (B. E. Dixon, 2016). Increasing providers' capability to **exchange** information electronically with other providers has the potential to help address existing gaps in health information sharing between healthcare providers. This goal of improving care coordination is central to the concept of HIE.

The Indiana Health Information Exchange (IHIE) makes statewide health record data available to physicians and researchers via the Indiana Network for Patient Care (INPC). The INPC was launched by Regenstrief Institute and is now supported by the IHIE (McDonald et al., 2005). As one of the oldest and largest health information exchange (HIE) infrastructures, the INPC has been shown to be a feasible data source to assess population health from electronic health records (EHR) (B. Dixon, Gibson, Frederickson, & Rosenman, 2014; B. E. Dixon, Whipple, Lajiness, & Murray, 2015) (Biondich et al., 2014). According to the Office of National Coordinator for Health

Information Technology an EMR contains the standard medical and clinical data gathered in one healthcare provider's office. By contrast, an EHR goes beyond the data collected at the individual providers' office and collects and includes a more comprehensive patient history (HealthIT.Gov).

The National Academy of Medicine defines the eight core functionalities of an EHR as: 1) health information and data, 2) result management, 3) order management, 4) decision support, 5) electronic communication and connectivity, 6) patient support, 7) administrative processes and reporting, and 8) reporting and population health (IOM, 2003).

Starting in 1980, the INPC contains 17.2 million individual patients, 4.6 billion clinical observations, and 165 million text reports capturing 68% of the state population in 2014. The INPC has institutional participation from over 80 hospitals in the state, major health networks, and major health insurance provider data, making the comprehensive statewide HIE well suited for research possibilities into project feasibility and allows for the construction of datasets for analysis (B. E. Dixon, 2016).

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## CHAPTER TWO: THEORETICAL FRAMEWORK

This chapter presents the guiding theoretical framework used to study living kidney donors in a statewide health information exchange (HIE). The chapter discusses important concepts of health policy and management and describes the context in which this dissertation is studied.

### Health Policy and Management

Public and population health can be influenced by various policies. The World Health Organization (WHO) defines health policy as “decisions, plans, and actions that are undertaken to achieve specific healthcare goals within a society” (WHO, 2016). According to the WHO, an explicit health policy can achieve many things, including a vision for the future that helps to set goals and metrics for the short, medium, and long-term. Furthermore, health policy outlines priorities and expected roles of different groups while building consensus and informs people. The U.S. Centers for Disease Control and Prevention defines ‘policy’ as a law, regulation, procedure, administrative action, incentive, or voluntary practice of governments and other institutions (CDC, 2015).

As healthcare is complex and dynamic, leaders must consider both internal and external influences that impact resources and activities of an organization. Health services administration and management has a role in health policy. One of the crucial areas for managing external influences is to be knowledgeable about health policy matters at the local, state and federal levels (Thompson, Buchbinder, & Shanks, 2005).

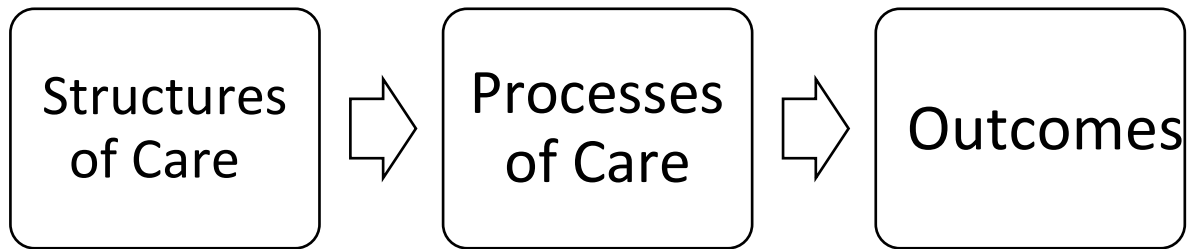
## Health Services Research

‘Health services research’ (HSR) is defined by AcademyHealth as the multidisciplinary field of scientific investigation that studies how social factors, financing systems, organizational structures and processes, health technologies, and personal behaviors affect access to healthcare, the quality and cost of healthcare, and ultimately our health and well-being (AcademyHealth, 2012). Within HSR, the domains include individuals, families, organizations, institutions, communities, and populations, and were first presented in the 2002 Agency for Healthcare Research and Quality definition of HSR (AHRQ, 2015).

## Donabedian Framework

The Donabedian Framework has been foundational to research in health services (Donabedian, 1966, 1978, 1988). In 1988 Donabedian (pg.1783) noted, “As we seek to define quality, we soon become aware of the fact that several formulations are both possible and legitimate.” Therefore quality measurement in healthcare can also be viewed as non-standardized (Pronovost, Miller, & Wachter, 2007). However, the standard conceptual model of healthcare quality that is most heavily cited is Donabedian (Donabedian, 1966, 1978, 1988). The Donabedian framework lays out three constructs of quality in causal fashion: structure, process, and outcome (Figure 2.1).

**Figure 2.1: Donabedian 3-Factor Conceptual Framework of Quality**



\*Adapted from Donabedian, 1988

In the Donabedian conceptual model, structure pertains to all capital that enables delivery of care including human, cultural, physical, but is not sufficient for the delivery of health services (Campbell, Fitzpatrick, Haines, & Kinmonth, 2000). Processes of care is often codified in clinical practice guidelines and can be measured as adherence as standard procedures which are recommended for a patient's condition. Process is the actual delivery of care and can be further broken down into technical and interpersonal dimensions (Blumenthal, 1996; Campbell et al., 2000; Donabedian, 1988; Steffen, 1988). Technical care is the application of clinical medicine to a personal health problem (Campbell et al., 2000; Donabedian, 1978) and is widely viewed as a credible measure of service quality for empirical research (Jha, Li, Orav, & Epstein, 2005). Interpersonal care can be seen as the interaction between the patient and members of the healthcare system and is a complementary measure of service quality (Fenton, Jerant, Bertakis, & Franks, 2012).

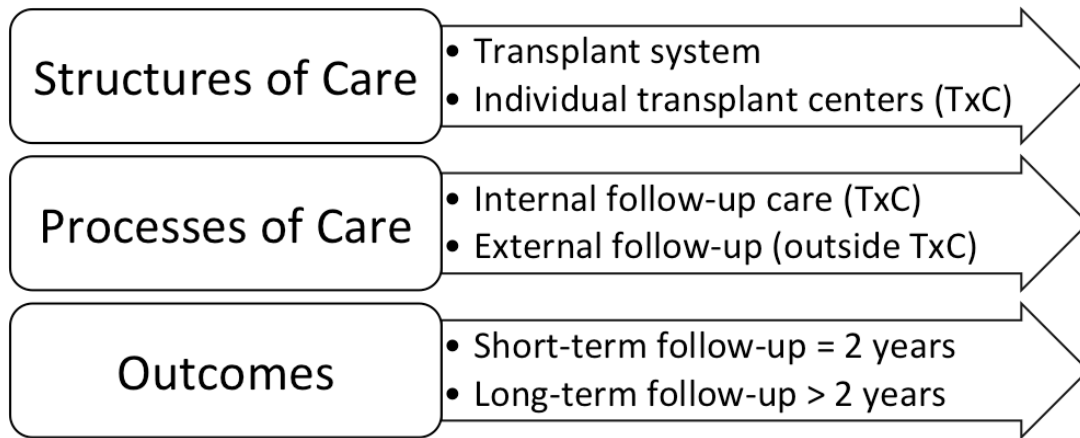
According to Donabedian (1988, pg. 1744) “interpersonal process is the vehicle by which technical care is implemented and on which its success. Therefore, the management of the interpersonal process is to a large degree tailored to the achievement

of success in technical care” (Donabedian, 1988). Finally, the Donabedian model focuses on outcomes, which are intended to measure patient health status after the service encounter (Donabedian, 1988). There are many outcome measures, (e.g. symptoms, quality of life, functional status, cost, post-care complications, risk-adjusted mortality and readmission rates, etc.) but not all are suitable for measuring delivered service quality (Krumholz et al., 2000).

#### Henderson Conceptual Model for Living Kidney Donor Follow-up

Adapting the Donabedian 3-factor conceptual framework of quality, a new model is presented to understand how structures of care, processes of care and outcomes are applied to living kidney donor follow-up. Figure 2.2 illustrates the Henderson Conceptual Model for Living Kidney Donor Follow-up. The structures of care can be viewed as both the national organ transplant system as well as the individual transplant centers performing the living donor transplant surgery that is responsible for reporting follow-up to the Organ Procurement and Transplantation Network under the United Network for Organ Sharing policies. Processes of care for living kidney donor follow-up can be viewed as both internal and external to the transplant center that is responsible for reporting; while transplant centers encourage living kidney donors to return to the transplant center for follow-up care, primary care supports the process of care from an external perspective. Outcomes for living kidney donor follow-up can be viewed as both short and long-term and vary in measures based on policy requirements and principles of prevention.

**Figure 2.2 The Henderson Conceptual Model for Living Kidney Donor Follow-Up**



\*TxC stands for Transplant Center

## Original Contribution

This dissertation will contribute to the existing literature by improving the understanding and impact of health information exchange (HIE) on retrospectively identifying presumed living kidney donors, understanding follow-up care patterns, and examining their health outcomes. Current processes often yield incomplete and untimely reporting across transplant centers requiring time-consuming efforts needed in the years after donation. New approaches are needed which will capitalize on new technology and new datasets in order to better understand new ways that living donor follow-up data can be collected. Given their significance to preventive care for long-term living donor health and safety, collecting high-quality, reliable, complete and timely data merits ongoing attention and quality improvement efforts. Additionally, there is evidence of growth with respect to implementation of information systems within public health (B. E. Dixon et al., 2015). This study is the first one to utilize HIE as a novel data source to study living kidney donation outcomes.

The dissertation seeks to address three distinct, but related, research questions which include: 1) Can a cohort of living kidney donors be retrospectively identified in a statewide HIE? 2) What follow-up care patterns are demonstrated in the HIE for the living kidney donor cohort? and 3) What clinical follow-up outcomes are associated with presumed living kidney donors in the identified cohort?

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### CHAPTER THREE: IDENTIFYING LIVING KIDNEY DONORS IN A STATEWIDE HEALTH INFORMATION EXCHANGE

#### Abstract

**Background:** Providing follow-up care for living kidney donors (LKDs) is an important responsibility that the transplant community must assume, but patients are often lost-to-follow-up.

**Objective:** This study sought to identify a cohort of LKDs in a repository of integrated, longitudinal medical records gathered using health information exchange (HIE) across a network of health systems.

**Methods:** Using a text-mining approach involving plaintext clinical notes, we identified a cohort of 1,245 LKDs. The cohort was refined by age exclusion based on transplant center level data.

**Results:** The LKD cohort identified showed high correlation with Organ Procurement and Transplantation Network LKD frequency by year ( $r = 0.948$ ), demonstrating that the methodology was effective for our sample population.

**Conclusion:** As HIE efforts expand across the nation, these repositories are valuable sources that be further explored for use in clinical and research scenarios to improve follow-up and involving patients who span many care providers.

**Keywords:** Registry-based studies; retrospective studies; living kidney donors; health information technology

## Introduction

According to Organ Procurement and Transplantation Network and United Network for Organ Sharing (OPTN/UNOS) data, there were 5,074 living kidney donors (LKDs) in 2015. Follow-up care for LKDs is paramount for patient safety and to promote national trust in the organ transplant system. Follow-up care at the transplant center has been required by OPTN/UNOS Policy 18 for two years post donation since 2013, with annual follow-up in primary care as the current clinical practice recommendation (D. A. Mandelbrot & Pavlakis, 2012; OPTN, 2016a). While difficult to achieve, successful strategies have been proliferated, recognizing that follow-up and continuity of care for LKDs is vital to the ethical obligation transplant centers have to promote patient safety in living donation (Dew et al., 2011). In addition to maintaining compliance with post-donation follow-up care policy, the ability to follow-up with LKDs post-donation provides organ transplant researchers and epidemiologists an opportunity to better understand the risks and sequelae of living donation thus ultimately improving informed consent.

Organ transplant data as a whole is traditionally robust, but is limited in the area of living donation. While nationally maintained data sources such as OPTN/UNOS (which provides data for the Scientific Registry of Transplant Recipients (SRTR)) are available, limitations in regards to living donation exist (Massie, Kuricka, & Segev, 2014; J. Schold et al., 2015). This is because prior reports have indicated a lack of complete reporting of LKD follow-up on standard OPTN/UNOS forms; follow-up is also highly variable by transplant center (D. Mandelbrot et al., 2007; D. A. Mandelbrot et al., 2009; J. Schold et al., 2015; Amy D Waterman et al., 2013).

Health information exchange (HIE) is the electronic transfer of clinical and administrative information across diverse and often competing health care organizations (Dixon, 2016). With a significant increase in the availability and use of HIE by hospitals catalyzed by federal policy (Blumenthal, 2010; Furukawa, Patel, Charles, Swain, & Mostashari, 2013), communities are developing the capability to exchange a wide range of data to support a growing number of purposes in health care delivery and public health. Previously, HIE has been shown to hold promise for population health measurement and tools from the discipline of clinical informatics, such as natural language processing (NLP), can be used in conjunction with HIE to develop cohorts for outcomes research (Dixon, Gibson, Frederickson, & Rosenman, 2014; Wang et al., 2015).

As HIE can connect components of the health system together in an effort to improve care coordination, HIE networks may be mechanisms in which a transplant center can identify donors who might otherwise be lost-to-follow-up. The objective of this feasibility study is to present a novel method for retrospectively identifying LKDs in a statewide HIE repository with tools from the discipline of clinical informatics. We describe HIE networks as a new clinical data source and the cohort identification process that has the potential to be replicated nationwide to improve LKD follow-up, coordination, and continuity of care.

## Methods

### *Data source*

The Indiana Network for Patient Care (INPC) represents one of the largest HIE networks in the country with over 100 separate healthcare entities providing data and

includes: major hospitals, health networks, and insurance providers (Biondich & Grannis, 2004; Overhage, 2016). The INPC also includes outpatient data from participating physician offices, community health and indigent care centers, county and state public health departments, national laboratories, payers, and ancillary sources such as radiology systems (Biondich & Grannis, 2004; McDonald et al., 2005). When combined, the information from these institutions represent data on over 17 million patients in the form of 4.9 billion clinical observations, 951 million encounter records, and over 195 million plaintext reports (Institute, 2015). The INPC is used by clinicians to facilitate real-time access to past medical history, and the associated HIE repository also facilitates access to data for researchers (Dixon, Whipple, Lajiness, & Murray, 2015; Dixon BE, 2016).

#### *Patient Population*

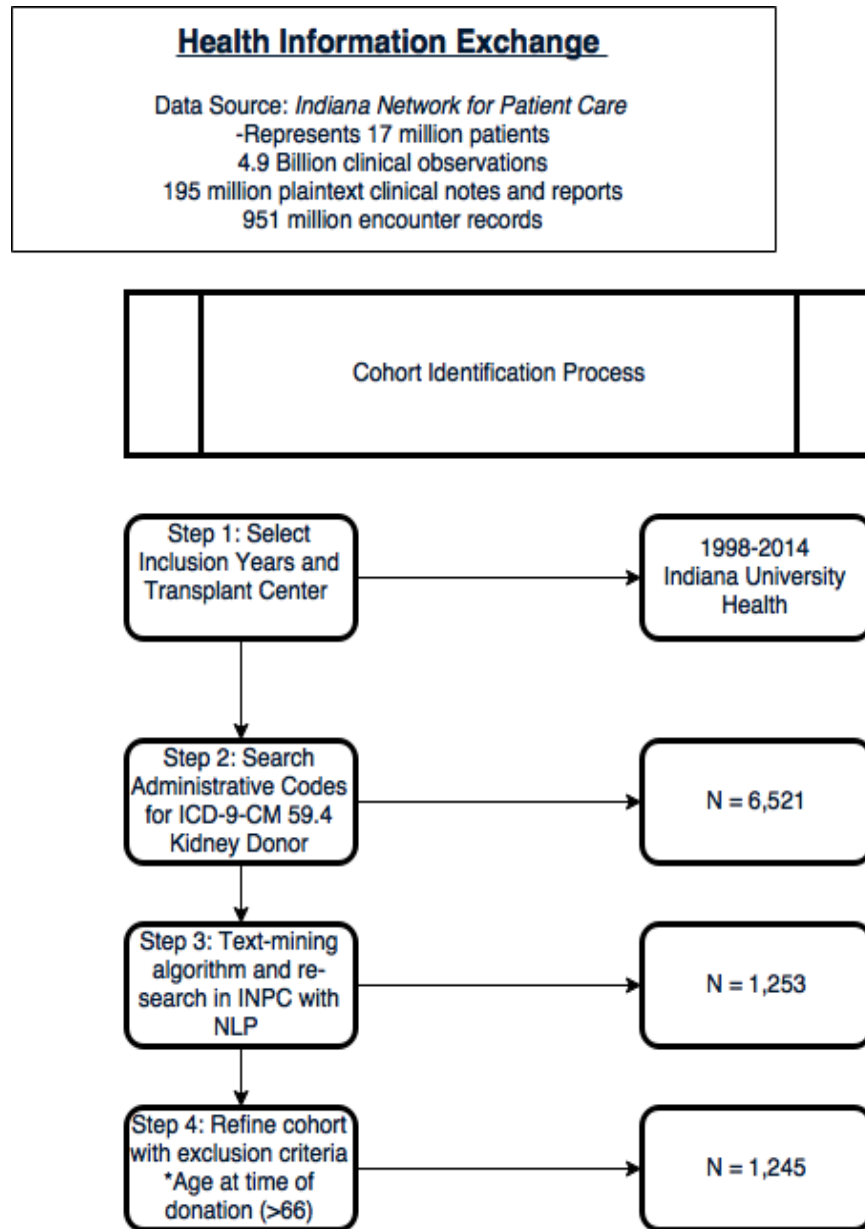
We sought to retrospectively identify LKDs from Indiana University Health, one of the participants in the INPC, between January 1, 1998, and July 22, 2015. Based on data from July 30<sup>th</sup>, 2015, Indiana University Health (formerly Clarian Health) has performed 90% of all LKD transplants in the state to date since the OPTN began collecting data in 1988 (1,708 out of 1,888 total living donor kidney transplants). The other transplant centers in the state, Lutheran Hospital in Fort Wayne and St. Vincent's Hospital in Indianapolis, did not begin performing LKD transplants until 2007 and 2009, respectively, according to 2015 OPTN annual state-level data.

### *Cohort Identification*

We used a combination of traditional and advanced methods to identify the LKD cohort as summarized in Figure 3.1. First, we employed a traditional health services research method of using administrative data, International Classification of Diseases Clinical Modification Ninth Revision (ICD-9-CM) diagnostic and Current Procedural Terminology (CPT) codes that are routinely captured in the INPC as patients traverse the health system. While administrative codes are sensitive, they are not specific enough to distinguish LKDs from other populations in the INPC such as deceased kidney donors and kidney transplant recipients. Therefore we developed a text-mining algorithm to identify LKDs within plaintext reports (e.g., clinical notes) using the Regenstrief NLP Tool<sup>®</sup> that employs dictionary-based named entity recognition. The text-mining algorithm uses a series of keywords as inputs to a process that searches across a set of plaintext reports to identify LKDs. The text-mining algorithm uses language from the Unified Medical Language System and considers spelling variants as well as negation when evaluating the contents of a plaintext report. Pre-processing (spell check, removal of duplicate characters, application of grammar rules) for word sense-disambiguation, lexical tokenization (breaking text into words, phrases), negation handling (detecting if an expression is negative), and stemming for word classification (i.e. wait – waiting) were included. (Bodenreider, 2004; Bushinak, AbdelGaber, & AlSharif, 2011; Lindberg, Humphreys, & McCray, 1993; Rink, Harabagiu, & Roberts, 2011; Witten & Frank, 2005). Appendix A contains the complete list of terms used to create the text-mining algorithm. The cohort was refined using transplant center data; we excluded records by

restricting for patient age ( $>67$  years old), as the oldest recorded donor, according to IU Health records, would be age 66.

**Figure 3.1 Cohort Identification Process**





### *Cohort Validation*

To validate that the cohort contained valid electronic health records for LKDs, we randomly sampled 100 (8%) unique patients for manual chart review. An experienced data analyst at the Regenstrief Institute familiar with INPC data examined patient charts to confirm that the individual was indeed a LKD as opposed to a deceased kidney donor or evidence of another medical purpose such as renal carcinoma. Counts of LKDs by year were compared to the publically available OPTN database which is the national ‘gold standard.’ OPTN data on LKDs come from a registration form submitted by the transplant center when they enter the transplant system.

### *Data Analysis*

Pearson’s correlation was performed to compare the INPC derived cohort of presumed LKDs with OPTN yearly counts. Analysis was carried out using SPSS, version 23 (IBM SPSS Statistics, Inc.). This study was approved by the Indiana University Institutional Review Board Study # 1506003825.

## **Results**

### *Cohort Identification and Internal Validation*

We identified 6,521 unique patients with ICD-9-CM V59.4 for ‘Kidney Donor’ using administrative data captured in the INPC. We attempted to also use CPT code 50320 for ‘Remove Kidney Living Donor,’ but it had never been used in INPC. The frequency of ICD-9-CM code V59.4 are presented by location in INPC in Table 3.1. The top three most frequent locations where ICD-9-CM V59.4 appear in INPC include

discharge diagnosis (N = 22,484) and hospital diagnosis (N = 16,712), and admitting diagnosis counts (N = 6,362). This administrative code only appeared 58 times in clinic billing diagnosis.

**Table 3.1 Frequency of ICD-9-CM V59.4 by Health Information Exchange Location**

<b>Locations</b>	<b>Count</b>
Discharge diagnosis	22,484
Hospital diagnosis	16,712
Admitting diagnosis	6,362
Initial diagnosis	158
Clinic billing diagnosis	58
Diagnosis & complaints	45
Hospital diagnosis	2

Source: Indiana Network for Patient Care (1998-2014)

The text-mining algorithm identified 1,253 unique patients. Of these patients, 1,196 (95%) also had an ICD-9-CM code v59.4 for Kidney Donor in their administrative records. Refining the cohort with transplant center data excluded eight patients based on age at time of donation (>67 years old), resulting in a final cohort of 1,245 presumed LKDs. Out of the 100 records sampled for internal validation, only one patient (1%) was not confirmed to be a LKD.

#### *Validation Against External Data*

Pearson's correlation showed a strong positive correlation between the INPC presumed LKD cohort and OPTN yearly counts ( $r = 0.948$ ;  $p < 0.00001$ ). Table 3.2 shows INPC presumed LKD counts by year and the corresponding proportion of OPTN counts.

**Table 3.2 Presumed Living Kidney Donor Cohort by Year and Proportion of Expected**

Year	HIE <sup>a</sup>	OPTN <sup>b</sup>	Proportion of Expected
1998	39	50	78%
1999	55	49	112%
2000	53	58	91%
2001	61	65	94%
2002	68	67	101%
2003	58	59	98%
2004	81	80	101%
2005	80	76	105%
2006	108	107	101%
2007	83	85	98%
2008	91	90	101%
2009	105	112	94%
2010	104	104	100%
2011	84	83	101%
2012	62	62	100%
2013	72	72	100%
2014 <sup>c</sup>	41	65	63%

Source: Indiana Network for Patient Care (1998-2014)

*N* = 1,245

Notes:

HIE = Health Information Exchange data from the Indiana Network for Patient Care

OPTN = Organ Procurement and Transplantation Network living kidney donor counts at the center level based on July 31<sup>st</sup>, 2015

### *Cohort Demographics*

The median and interquartile range (IQR) age at donation was 40.4 years (32-49) (range=19-66). Table 3.3 presents cohort demographics and by age, sex, and race. The majority of presumed LKDs were white 87.9%, 89 (7.9%) were Black or African-American, and 26 (2.2%) were Hispanic. There were 27 (2.2%) reported as ‘other’ or ‘unknown’ race and only one presumed LKD reported as Asian and one as Native Hawaiian or Pacific Islander. Six (0.5%) had missing racial data.

**Table 3.3 Presumed Living Kidney Donor Cohort Demographics**

	Mean	S.D.
<b>Age</b>	40.4	10.7
Female (N = 739)	41.8	10.4
Male (N = 506)	38.5	10.7
<b>Race</b>		
White (N = 1,094)	41.0	10.6
Black (N = 89)	36.2	9.8
Hispanic (N = 26)	34.4	9.4
Asian (N = 1)	+	+
Native-American Pacific Islander (N = 1)	+	+

Source: Indiana Network for Patient Care, 1998-2014

Notes: + category is too small to report values

## Discussion

We present a novel method for the identification of LKDs from an HIE network that might be otherwise lost-to follow-up. This feasibility study makes an important step forward in understanding how LKDs who may have already left the transplant system for care can best be identified for follow-up and coordination of care. Our identification method resulted a cohort of 1,245 LKDs who donated a between 1998 and 2014 for which we were able to validate against national registry data which is the current gold standard. Text-mining was preferred over ICD-9-CM administrative code v59.4 for identifying LKDs in INPC. In our sample, ICD-9-CM administrative coding did not allow for the easy identification of LKDs. ICD-9-CM codes were not specific enough for identifying LKDs from other populations, including deceased kidney donors, recipients

of a kidney transplant, and patients undergoing nephrectomy for presumed other causes. Our text-mining algorithm allowed for the identification of LKDs that significantly correlates with LKD counts reported nationally by the OPTN providing confidence in our methodology.

Implications for LKD cohort identification using a HIE network can improve how individual centers and the national transplant community nationally provide follow-up, surveillance, care coordination, and continuity of care. In 2011, a consensus conference of experts emphasized the importance of long-term follow-up of living donors and concluded that living donor follow-up would be improved with more data from different sources and mechanisms for better data collection, submission, and analysis of data on live donors (Leichtman et al., 2011). As a new data source for transplant centers, we believe HIE could help improve follow-up reporting, data collection, and continuity of care. HIE could also reduce significant barriers reported that prevent longitudinal follow-up such as including inconvenience, lack of donor desire for follow-up *at the transplant center*, and out-of-date donor contact information (Amy D Waterman et al., 2013). We view the current federal incentives for meaningful use and interoperability of electronic health records to be supportive of the expert recommendations set forth in 2011 to improve living-donor follow-up care (Leichtman et al., 2011; Office of the National Coordinator for Health Information Technology & Human, 2010).

HIE networks contain integrated clinical data both internal and external to the transplant center, which represents two processes of care for LKD follow-up and the opportunity to examine both short and long-term outcomes (See Chapter 3, Conceptual Framework). Cohort identification through HIE presents an new opportunity to

investigate post-donation outcomes in living donors by understanding their follow-up care patterns at the transplant center for the two year period following the donation, as well as the care they receive external to the transplant system. Previously, external data sources such as pharmacy and private claims data have been previously linked with OPTN data in order to study depression, cancer diagnosis, post-donation narcotic use, and morbidity associated with racial variation in living kidney donors (Lentine et al., 2015; Lentine, Schnitzler, et al., 2012; Lentine et al., 2010; Lentine, Vijayan, et al., 2012).

With nearly half of U.S. hospitals currently participating in data sharing with EHRs and several others are working towards building this capacity (Adler-Milstein, Bates, & Jha, 2011), improving identification, follow-up and care continuity for LKDs will become easier. In addition, large transplant centers might collaborate to create a clinical data and patient-powered research network for LKDs, which are currently receiving attention and large financial investments. As an example, the Patient Centered Outcomes Research Institute recently approved \$142.5 million in funding to support 34 clinical research data networks supported through integration with the National Patient-Centered Clinical Research Network (PCORnet), a highly representative, national network for conducting clinical outcomes research (Fleurence et al., 2014; Stencel, 2015).

There are limitations that deserve mention in this feasibility study. First, we were limited in identifying LKDs in 2014 because of a time lag in the Regenstrief NLP Tool®. We ran the text-mining algorithm in July of 2015, but the last unique LKD we retrieved had a donation date in May of 2014. This limitation resulted in the proportion of expected

LKDs for this year being lower than if we were able to include donors through December of 2014; the yearly donor count in OPTN included the entirety of 2014. Second, while we believe that the validation for our cohort identification method was reasonable in this feasibility study, future studies should investigate formal F-measures performing sensitivity and specificity analysis to attain performance characteristics (precision, recall, accuracy) of the text-mining algorithm. *Recall*, or sensitivity, is the percentage of LKDs that were correctly identified by the algorithm. *Precision*, or positive predictive value, is the percentage of LKDs identified by the algorithm that are correct. *F-measure* is the harmonic mean of precision and recall, and provides a measure of overall accuracy (Chowdhury, 2010; Manning, Raghavan, & Schütze, 2008; Manning & Schütze, 1999). Finally, this feasibility study was limited to one transplant center and one HIE. The Indiana Health Information Exchange is a nationally recognized example of an advanced HIE infrastructure. Thus, the generalizability of using this data source is a potential limitation as other states have less robust infrastructures. However, the financial incentive to build out these exchanges exists nationwide (Adler-Milstein & Jha, 2012). Over half a billion dollars has been invested into state governments to support the technical development of HIE since 2009 (Williams, Mostashari, Mertz, Hugin, & Atwal, 2012). There are 56 current development projects to create similarly scaled infrastructures to support meaningful use and interoperability standards (HealthIT.Gov, 2014). For example, in New York where there were 510 LKDs in 2014, (10.8% of 5,538 total living kidney donations) adoption of HIE has been increasingly popular. In a statewide survey, some 98% of responding New York hospitals (N = 126) had implemented or begun

implementing an EHR which is greater than a fourfold increase in three years (Abramson, Silver, & Kaushal, 2014).

Currently, mechanisms and the authority exist for the Health Resources and Services Administration (HRSA) to fund long-term living donor data collection within the existing SRTR database. There is now an unambiguous endorsement from the transplant community supporting the clinical, scientific and administrative necessity to begin the development of a national registry. As reported at the November 17<sup>th</sup> 2015 public meeting of the Advisory Committee on Organ Transplantation, with the recent renewal of the federal contract the SRTR is now conducting a feasibility study for the development of a National Living Donor Registry with initial results due to HRSA in June of 2016 (Kaiskie, 2015). At the time of this writing, the SRTR is currently concluding the study (Personal Communication from SRTR, April 5th, 2016). Future investigations into the legal barriers and data use agreements in order to link datasets populated with HIE with existing SRTR to better understand the approximately 100,000 LKDs currently living in the United States is warranted.

## Conclusion

This feasibility study of a novel method for LKD cohort identification in HIE can enable transplant centers to find donors who might otherwise be deemed as lost-to-follow-up. Future research should formally assess the validity of the text-mining algorithm for the identification of LKDs when applied to another statewide HIE. As an existing infrastructure that enables pooled clinical data to improve care continuity, HIE can impact both processes and outcomes of follow-up care for LKDs. HIE data applications could also be useful in developing control cohorts for improved research on



long-term health outcomes such as demonstrating LKD longitudinal donation renal function trajectories and assessing the effectiveness of center-level screening of LKD candidates.

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## CHAPTER FOUR: LIVING KIDNEY DONOR FOLLOW-UP IN A STATEWIDE HEALTH INFORMATION EXCHANGE

### Abstract

**Background:** Follow-up care is important to promote patient safety and informed consent for living kidney donors (LKDs), but has been historically difficult to achieve. In 2013, the Organ Procurement and Transplantation Network/United Network for Organ Sharing implemented policy requiring that transplant centers provide two-year follow-up care for LKDs.

**Objective:** To assess receipt of 24-month (two-year) follow-up and differences by race and age in a cohort of LKDs identified in a health information exchange.

**Participants:** Electronic medical records of 1,245 patients 19 - 66 years old who donated a kidney between 1998 and 2014.

**Methods:** Binomial logistic regression was performed to ascertain the effects of age and race on receipt of 24-month follow-up controlling for the era in which the donation year occurred.

**Outcome Measures:** Receipt of 24-month follow-up was measured by timely and complete 24-month follow-up kidney laboratory data. Serum creatinine (SCr) and urinalysis (UA) were binary dependent categorical variables (yes/no).

**Results:** LKDs between the ages of 40 – 49 have are 1.3 times more likely of having 24-month follow-up, while those aged 50 – 59 are 1.8 times more likely as compared to 19-39 year olds. LKDs in the third donor era (2009-2012) were 65.1 times more likely to have 24-month follow-up than those who donated before 2004 while those LKDs in the



fourth era (2013-2014) were 22.2 times more likely than those donating between 1998 and 2004 to receive 24-month follow-up ( $p = 0.000$ ). Black or African-American LKDs were about twice as likely than those non-black or African-Americans to have 24-month follow-up ( $p = 0.014$ ).

Conclusions: This study provides previously unknown information about historical trends and differences in LKD follow-up care by age and race, where the most significant differences on receipt of 24-month follow-up was age. Knowledge of age-related differences in LKD follow-up care patterns at the transplant center level can assist research teams in the design and development of interventions to improve care and patient outcomes.

Keywords: living donation, health services, and registry-based studies

## Introduction

There are over 5,500 living kidney donors (LKD) entering the organ transplant system each year, but historically follow-up care has been difficult to achieve. The benefits of LKD follow-up include improved information that can be communicated to prospective donors about risks of donation, improved health and outcomes for living donors nationally, and improved national trust in the living donation process (Amy D Waterman et al., 2013). The Organ Procurement and Transplantation Network (OPTN)/United Network for Organ Sharing (UNOS) has collected follow-up data on living donors at 6 months and 12-months (1-year) post-donation since 1999, including information on serum creatinine (SCr), blood pressure, and body mass index (Brown Jr, Higgins, & Pruett, 2009). Although the OPTN/UNOS was collecting short-term follow-up data on living donors, one study revealed that in 2006 50% of LKDs had incomplete complication data at one year, and approximately one-third of LKDs were reported “lost to follow-up” (Klein et al., 2010).

In an effort to improve follow-up care patterns nationally, the OPTN implemented new policy requirements for transplant programs in order to promote consistency in the informed consent, medical and psychosocial evaluation, and follow-up of living donors in February of 2013. These new policies required transplant centers to submit ‘timely and complete’ follow-up including clinical and laboratory data for LKDs at the following three time points post-donation: 6-months, 12-months, and 24-months (OPTN, 2016d). ‘Timely and complete reporting and submission of data is defined by the OPTN as 60 days before or after the 6-month, 12-month, or 24-month anniversary of the donation date. Under the new OPTN/UNOS policy implemented in 2013, transplant centers must

report accurate, complete and timely follow-up data for *donor status and clinical information* for at least 60% of LKDs who donate between February 1, 2013 and December 31<sup>st</sup> 2014, 70% of LKDs who donated between January 1, 2014 and December 31<sup>st</sup> 2014, and 80% of LKDs who donated after December 31<sup>st</sup> 2014. In addition to donor status and clinical information, complete and timely follow-up for *kidney laboratory data* for at least 50% of LKDs who donate between February 1, 2013 and December 31<sup>st</sup> 2014, 60% of LKDs who donated between January 1, 2014 and December 31<sup>st</sup> 2014, and 70% of LKDs who donated after December 31<sup>st</sup> 2014 is mandatory. The required kidney laboratory data for follow-up includes serum creatinine (SCr) and urine protein (OPTN, 2016d). Two year, or 24-month follow-up is now considered to be the standard of care for all prospective donors and is considered the final required routine follow-up care visit to the transplant center before the LKD is released to the care of their primary care physician.

Nationally, efforts are being made to identify morbidity in the postoperative period and to facilitate the potential need for post-donation interventions for LKDs including those aimed at improving follow-up (A. X. Garg et al., 2012; H. N. Ibrahim et al., 2009; Lentine & Patel, 2012; P. Reese et al., 2014; Segev et al., 2010). These national efforts including the ability to monitor, identify, and facilitate population health management of LKDs at the transplant center-level has historically been limited by lack of infrastructures and processes in order to collect clinical data long after the short term surgical complication period has ended. As the ideal approach to capturing clinical data to improve knowledge about LKD health outcomes undergoes increasing debate amongst the transplant community and regulatory bodies, it is prudent to investigate new clinical

data sources including statewide health information exchange (HIE). As these new sources are available providing LKD data, patient level differences in follow-up care patterns can now be examined. Examination of follow-up care patterns can improve population health management and support the design of targeted interventions to improve post-donation follow-up at the transplant center level. The objective of this retrospective cohort study is to assess receipt of 24-month follow-up for LKDs including differences in race and age.

## Methods

### *Data Source*

INPC is the database of clinical and other information that is exchanged through the Indiana HIE and is derived from a variety of pooled Electronic Health Record (EHR) systems (Biondich & Grannis, 2004). INPC represents one of the largest patient networks in the country with over 100 separate healthcare entities providing data including: major hospitals, health networks, and insurance providers. INPC also includes outpatient data from participating physician offices, community health and indigent care centers, county and state public health departments, national laboratories, payers, and ancillary sources such as radiology systems (Biondich & Grannis, 2004; McDonald et al., 2005). When combined, the pooled information from these institutions represent data on over 17 million patients in the form of 4.9 billion clinical observations, 951 million encounter records, and over 195 million multimedia reports (Institute, 2015).

### *Study Participants*

Indiana University Health is one of three operational transplant centers in the state of Indiana and has performed over 90% of living kidney donor transplants since the

OPTN began collecting data in 1988. Assessment of 24-month follow-up included 1,245 LKDs with a donation date between January 1998 and May 2014. The Indiana University Institutional Review Board Study approved this study #1506003825.

### *Outcome Measures*

Receipt of 24-month follow-up was measured by kidney laboratory data and included serum creatinine (SCr) and urine protein measured by a urinalysis (UA) (OPTN, 2016e). In accordance with what is written in OPTN/UNOS policy, timely and complete follow-up laboratory data was defined as within 60 days of the 24-month donation anniversary.

### *Independent Variables*

Age categories were defined as 19-39 years old, 40-49 years old, 50-59 years old, and age 60 and over. Race was classified as either African-American or non-African-American (including Asian, Native American Pacific Islander, or White); ‘Null or code not mapped’ and ‘other or unknown’ were marked as missing data. Donation era was calculated based on year of donation and was stratified by four categories where 1998-2004 was the first donor ear; 2005-2008 was the second; 2009-2013 was the third; and 2013-2014 was the fourth.

### *Data Analysis*

The yearly proportion and frequency of LKDs with follow-up kidney laboratory data was identified in INPC for each donation year represented by the cohort. Binomial logistic regression was performed to assess receipt of 24-month follow-up differences including age and race while controlling for the era in which the donation year occurred.

A sensitivity analysis was conducted whereby donation year was categorized in multiple ways and is presented in Appendix B. This analysis was done due to the belief that there may be complex relationships between receipt of follow-up and time. First, there is a known increase in follow-up rates over time (Parente et al., 2015; J. Schold et al., 2015). Second, INPC data may be more complete over time, with a particular increase in completeness occurring in 2004 when the Indiana Health Information Exchange became incorporated and its infrastructure improved. Therefore, our sensitivity analyses categorized donation year in multiple ways in an attempt to account for these time trends and minimize confounding in our estimation of the relationship between receipt of follow-up and age and race. All data management and analyses were carried out with SPSS, version 23 (IBM SPSS Statistics, Inc.) and SAS, version 9.3 (SAS Institute, Cary, NC, USA) with a 95% confidence level where ( $p < 0.05$ ) is considered significant.

## Results

The median interquartile range (IQR) age at donation for the cohort ( $N = 1,245$ ) was 40.4 years (32-49). There were 739 female (59.4%) and 506 male (40.6%) LKDs and 89 (7.0%) were Black or African-American. There were 392 (31.4%) LKDs with 24-month SCr follow-up kidney laboratory data but only 40 (3.1%) had 24-month UA follow-up kidney laboratory data. As illustrated in Table 4.1, 2012 had the highest proportion of LKDs (79.4%) with 24-month SCr follow-up kidney laboratory data. There was no donation year with greater than a 7% proportion of LKDs with 24-month UA follow-up kidney laboratory data as shown in Table 4.2.

Binomial logistic regression models were analyzed to predict receipt of 24-month follow-up using age at time of donation, race, and donation era as predictors. Table 4.3 presents crude age and race differences in 24-month follow-up laboratory data. For receipt of 24-month follow-up as measured by SCr kidney laboratory data, a test of the full model against a constant only model was statistically significant, indicating that the predictors as a set reliably distinguished between LKDs with 24-month follow-up SCr laboratory data (chi square = 434.171,  $p < 0.000$  with  $df = 7$ , Nagelkerke's  $R^2 = .0.422$ ). Prediction success for the 24-month follow-up SCr laboratory data was 78.1%. The Wald criterion demonstrated that the age variable made a significant contribution to the prediction ( $p = 0.003$ ). Results of the binomial regression for receipt of 24-month follow-up as measured by SCr kidney laboratory data is presented in Table 4.4.

**Table 4.1 Living Kidney Donor Follow-Up at 6-month, 12-month and 24-months: Serum Creatinine**

<b>Donation Year</b>	<b>Total LKDs in Year</b>	<b>6 –month SCr</b>	<b>12 –month SCr</b>	<b>24 –month SCr</b>
1998	N = 39	17 (43.6%*)	0 (0.0%)	0 (0.0%)
1999	N = 55	49 (89.1%)	6 (10.9%)	4 (7.3%)
2000	N = 53	41 (77.4%)	2 (3.8%)	2 (3.8%)
2001	N = 61	48 (78.7%)	2 (3.3%)	1 (1.6%)
2002	N = 67	48 (71.6.4%)	3 (4.5%)	1 (1.5%)
2003	N = 58	51 (87.9%)	3 (5.2 %)	1 (1.7%)
2004	N = 82	82 (100.0%)	7 (8.5%)	4 (4.9%)
2005	N = 80	79 (98.8%)	7 (8.8%)	9 (11.3%)
2006	N = 108	108 (100.0%)	6 (5.6%)	11 (10.2%)
2007	N = 83	82 (98.8%)	10 (12.0%)	8 (9.6%)
2008	N = 91	89 (97.8%)	61 (67.0%)	60 (65.9%)
2009	N = 105	102 (97.1%)	73 (69.5%)	73 (69.5%)
2010	N = 103	98 (95.1%)	70 (68.0%)	56 (54.4%)
2011	N = 104	84 (80.8 %)	54 (64.3%)	62 (73.8%)
2012	N = 63	62 (98.4%)	40 (64.3%)	50 (79.4%)
2013	N = 72	72 (100.0%)	40 (63.5%)	48 (66.7%)
2014	N = 41	41 (100.0%)	34 (82.9%)+	2 (4.9%)+
<i>Total Cohort (All Years)</i>	N = 1245	1,153 (92.6%)	439 (35.3%)	392 (31.4%)

Source: 1998-2014 Indiana Network for Patient Care  
N = 1,245

Notes: LKD(s) = living kidney donor(s); SCr = serum creatinine laboratory test

\*% Proportion of total living kidney donors with serum creatinine laboratory test at each time point in comparison to the total number of donors in that year

+ Includes only LKDs with a donation date before May 2014



**Table 4.2 Living Kidney Donor Follow-Up at 6-month, 12-month and 24-months: Urinalysis**

Donation Year	Total LKDs in Year	6 –month UA	12 –month UA	24 –month UA
1998	N = 39	5 (12.8%*)	0 (0.0%)	0 (0.0%)
1999	N = 55	7 (12.7%)	2 (3.6%)	3 (5.5%)
2000	N = 53	12 (22.6%)	1 (1.9%)	1 (1.9%)
2001	N = 61	16 (26.2%)	0 (0.0%)	0 (0.0%)
2002	N = 67	11 (16.4%)	0 (0.0%)	0 (0.0%)
2003	N = 58	11 (19.0%)	0 (0.0%)	1 (1.7%)
2004	N = 82	14 (17.1%)	1 (1.2%)	1 (1.2%)
2005	N = 80	14 (17.5%)	0 (0.0%)	5 (6.3%)
2006	N = 108	20 (18.5%)	1 (0.9%)	1 (0.9%)
2007	N = 83	7 (8.4%)	2 (2.4%)	1 (1.2%)
2008	N = 91	6 (6.6%)	4 (4.4%)	4 (4.4%)
2009	N = 105	14 (13.3%)	6 (5.7%)	7 (6.7%)
2010	N = 103	12 (11.7%)	9 (8.7%)	7 (6.8%)
2011	N = 104	10 (11.9%)	2 (2.4%)	3 (3.6%)
2012	N = 63	5 (7.9%)	3 (4.8%)	4 (6.3%)
2013	N = 72	11 (15.3%)	0 (0.0%)	2 (2.8%)
2014	N = 41	3 (7.3%)	0 (0.0%)+	0 (0.0%)+
<i>Total Cohort (All Years)</i>	N = 1245	178 (14.3%)	31 (2.5%)	40 (3.1%)

Source: 1998-2014 Indiana Network for Patient Care

N = 1,245

Notes:

LKD(s) = living kidney donor(s); UA = urinalysis laboratory test to measure urine protein

\*% Proportion of total living kidney donors with urinalysis laboratory test at each time point in comparison to the total number of donors in that year + Includes only LKDs with a donation date before May 2014

**Table 4.3 Crude Age and Race Differences in 24-Month Follow-Up Kidney Laboratory Data in a Statewide Health Information Exchange**

<b>Race</b>	<b>SCr 24-Month</b>	<b>UA 24 –Month</b>
<u>All Races</u>	% (OR)	% (OR)
<i>Age 19-39</i>	30% (0.84)	4% (1.84)
<i>Age 40-49</i>	28% (0.82)	2% (0.49)
<i>Age 50-59</i>	37% (1.33)	3% (0.91)
<i>Age 60+</i>	56% (2.86)	2% (0.71)
<u>Black or African-American</u>		
<i>Age 19-39</i>	32% (0.33)	3% (0.22)
<i>Age 40-49</i>	58% (2.48)	21% (9.07)
<i>Age 50-59</i>	60% (2.45)	0% (0.00)
<i>Age 60+</i>	--	--
<u>Non-Black or African-American</u>		
<i>Age 19-39</i>	30% (0.89)	4% (2.38)
<i>Age 40-49</i>	27% (0.74)	1% (0.22)
<i>Age 50-59</i>	36% (1.34)	3% (1.11)
<i>Age 60+</i>	58% (3.13)	3% (0.84)

Source: 1998-2014 Indiana Network for Patient Care

*N* = 1,245

SCr = serum creatinine; UA = urinalysis

**Table 4.4. Results of a Logistic Regression Model of 24-Month Follow-Up for Living Kidney Donors with Serum Creatinine Kidney Laboratory Data**

Variable	Coefficient ( $\beta$ K; log-odds)	Standard error	Odds Ratio <sup>a</sup> (OR)	Lower 95% CL <sup>c</sup>	Upper 95% CL	Wald chi- square	p- value <sup>b</sup>
<b>Age</b> (19-39)						13.971	0.003*
40-49	0.294	0.182	1.3	0.940	1.916	2.614	0.106
50-59	0.584	0.199	1.8	1.213	2.652	8.586	0.003*
60+	1.090	0.398	3.0	1.363	6.489	7.502	0.006*
<b>Race</b> (Non-black or African- American) Black or African- American	0.685	0.278	2.0	1.150	3.418	6.073	0.014*
<b>Donor Era</b> (1998-2004)						248.079	0.000
2005-2008	2.220	0.309	9.2	5.022	16.879	51.538	0.000
2009-2012	4.175	0.307	65.1	35.634	118.795	184.768	0.000
2013-2014	3.098	0.344	22.2	11.284	43.481	81.035	0.000

Source: 1998-2014 Indiana Network for Patient Care

Notes: N = 1,212

Reference categories are in parentheses

a. Odds ratio =  $e^{\log\text{-odds}} = e^{\beta}$ . Also known as relative odds.

b. Test statistics and p-values pertain to both coefficients (log-odds) and odds ratios.

c. CL = Confidence limit. The 95% confidence limits for the coefficient (log-odds) can be calculated as  $\beta \pm (1.96 \times \text{standard error})$ . The confidence limits for the log odds ration are calculated  $e^{\beta \pm (1.96 \times \text{standard error})}$ 

Based on SCr kidney laboratory data, LKDs between the ages of 40 – 49 had a 1.3 times greater odds of having 24-month follow-up, while those aged 50 – 59 had 1.8 times greater odds as compared to 19-39 year olds. LKDs aged 60 or above at the time of donation had a three times the odds of having 24-month follow-up as compared to younger donors under 40. Donor era significantly contributed to the prediction. As compared to LKDs in the first donor era (1998-2004), those in the second data era (2005-

2008) had 9.2 greater odds of receipt of 24-month follow-up. Those LKDs in the third donor era (2009-2012) had 65.1 times greater odds of 24-month follow-up than those who donated before 2004. Those LKDs in the fourth era (2013-2014) had 22.2 times greater odds than those donating between 1998 and 2004 to receive 24-month follow-up ( $p = 0.000$ ). Black or African-American LKDs had about two times greater odds than those non-black or African-Americans to have 24-month follow-up ( $p = 0.014$ ) based on SCr kidney laboratory data.

For the assessment of 24-month follow-up based on UA kidney laboratory data, a test of the full model against a constant only model was statistically significant, indicating that the predictors as a set reliably distinguished between LKDs with UA 24-month follow-up laboratory data (chi square = 18.132,  $p < 0.042$  with  $df = 7$  Nagelkerke's  $R^2 = .060$ ). Prediction success for the 24-month follow-up with UA laboratory data was 96.8%. The Wald criterion demonstrated that age ( $p = 0.502$ ) and race ( $p = 0.079$ ) did not significantly contribute to the prediction, however, donation era was significant in this model ( $p = 0.009$ ). LKDs in the third data era (2009-2012) had four times greater odds of to having 24-month follow-up than those who donated in the first era (1998- 2004) as presented in Table 4.5.

For sensitivity analysis of the donation era variable additional binomial logistic regression models were built to compare receipt of 24-month follow-up based on how the donation year variable was stratified. In the sensitivity analysis, models with three or four donation year categories dominated those with only two donation eras. As the odds and significance of age and race variables were robust in all models that stratified the donation year variable before and after the year 2004, a four-category donation era

specification was selected for the final model presented. Of note, there was a change in the impact of the oldest age group (age 60 and older) on receipt of 24-month follow-up when the specifications for the donation years were changed potentially reflecting a correlation between donation year and LKD age.

**Table 4.5. Results of a Logistic Regression Model of 24-Month Follow-Up for Living Kidney Donors with Urinalysis Kidney Laboratory Data**

Variable	Coefficient ( $\beta$ ; log-odds)	Standard error	Odds Ratio (OR) <sup>a</sup>	Lower 95% CL <sup>c</sup>	Upper 95% CL	Wald chi- square	<i>p</i> -value <sup>b</sup>
<b>Age</b>						2.357	0.502
(19-39)							
40-49	-0.654	0.439	0.52	0.220	1.228	2.225	0.136
50-59	-0.205	0.443	0.82	0.342	1.940	0.215	0.643
60+	-.0516	1.044	0.60	0.077	4.615	0.245	0.621
<b>Race</b>							
(Non-black or African- American)							
Black or African- American	0.822	0.469	2.3	0.908	5.699	3.079	0.079
<b>Donor Era</b>						11.498	0.009*
(1998-2004)							
2005-2008	0.537	0.525	1.7	0.612	4.786	1.049	0.306
2009-2012	1.377	0.471	4.0	1.574	9.980	8.543	0.003*
2013-2014	0.155	0.828	1.2	0.231	5.916	0.035	0.851

Source: 1998-2014 Indiana Network for Patient Care

Notes: *N* = 1,212

Reference categories are in parentheses

a. Odds ratio =  $e^{\log\text{-odds}} = e^{\beta}$ . Also known as relative odds.

b. Test statistics and *p*-values pertain to both coefficients (log-odds) and odds ratios.

c. CL = Confidence limit. The 95% confidence limits for the coefficient (log-odds) can be calculated as  $\beta \pm (1.96 \times \text{standard error})$ . The confidence limits for the log odds ration are calculated  $e^{\beta \pm (1.96 \times \text{standard error})}$

## Discussion

Binomial logistic regression models show that LKD age at time of donation is significantly associated with receipt of 24-month follow-up. With respect to age, younger donors (under the age of 40) have lower odds of having 24-month SCr follow-up kidney laboratory data, a clinical value used to measure renal function compared to older donors. Black or African-American LKDs have two times greater odds as non-Black or African-Americans to have received 24-month follow-up. Donation era was a significant predictor of receipt of 24-month follow-up based on SCr and UA kidney laboratory data as LKDs, with donation dates before 2004 having lower odds of having 24-month follow up than those who donated after 2004. Follow-up at 24-months significantly improved between 2005 and 2008 and again between 2009 and 2012. Donors in the fourth donation era (2013 and 2014) had about 22 times greater odds than for those who donated between 1998 and 2004 to have 24-month follow-up. Findings suggest that LKD follow-up has improved over time and changes in OPTN policy have led to an improvement in 24-month follow-up. The proportion of LKDs within each donation year with timely and complete 24-month follow-up has increased over time and is reflected in this transplant-center level cohort. Furthermore, these findings suggests and reflects that participation in the collection and reporting of patient data to INPC has evolved over time, and especially since improvements to the technical operation of the statewide HIE were implemented by the end of 2004.

Follow-up care is important for continued patient safety in live donation, as well as for transplant center compliance with OPTN/UNOS policy (OPTN, 2016e). This study provides additional evidence of what has been previously described by Schold et al.

(2012) regarding LKD follow-up including associations of age and the capture of post-donation follow-up data (J. D. Schold et al., 2012). With data from the Scientific Registry for Transplant Recipients, the presence of follow-up data was recently shown to be highly variable by individual transplant center, with only 30 - 40% of known variation in missing data explained at the transplant center level (J. Schold et al., 2015). In this same national study, differences in complete follow-up were most dramatic by donor age, race, educational attainment, distance between donors' residence, and the transplant center, and size of the living donor program (J. Schold et al., 2015). Other previous studies described missing follow-up data to be associated with characteristics that increase LKD risk for future medical problems including the development of chronic conditions such as diabetes and hypertension (Lentine & Patel, 2012). Incomplete follow-up may reflect both patient and transplant center factors, including variable infrastructure and processes in which follow-up care is provided (D. A. Mandelbrot et al., 2009; J. Schold et al., 2015). Previous studies have shown missing follow-up data to be correlated with LKDs residing longer distances from the transplant center for which the donation took place (J. Schold et al., 2015).

Knowledge of age and racial differences in complete and timely follow-up care for LKDs explored in this study provides valuable information for transplant centers and research teams recognizing the need to develop new behavioral and technological interventions to improve follow-up care. Transplant centers can use knowledge of current follow-up care patterns in the planning and development of implementation strategies designed to improve follow-up care processes at the administrative and regulatory compliance level. As such, evidence that younger LKDs are less likely to have timely and

complete post-donation follow-up can help transplant centers in the creation of patient-centered messages that reinforce that follow-up care is essential for donor safety, clinical care, and improved informed consent.

There are several limitations to this study that deserve mention. While LKDs with a donation year in 2013 and 2014 were included for analyses, not all donors from these years have 24-month follow-up laboratory data available in INPC based on the date of our data query and our inability to capture LKDs past May of 2014 (See Chapter 3). Importantly, the presence or absence of LKD follow-up kidney laboratory data does not necessarily mean that follow-up care *did* or *did not* occur. Our study uses the policy language of ‘timely and complete’ in deeming kidney laboratory data as a proxy for receipt of 24-month follow-up. LKDs who may have received follow-up that occurred outside of the 60-day window after the 24-month anniversary of the donation date were not included in this analysis. Analysis of 24-month follow-up is limited by the data source, meaning that a donor must have received follow-up from an institution participating in INPC. As INPC is primarily a statewide clinical data source, it may not capture data on LKDs who left the state and received follow-up care. Finally, there is the possibility that kidney-specific labs were performed, but were not subsequently reported to the transplant center. While this is not a significant limitation to our understanding of receipt of 24-month follow-up in this analysis, routine UA laboratory data was limited in INPC in comparison to SCr laboratory data in this study (See Table 4.1 and Table 4.2). Routine UA results are further difficult to clinically quantify and discern (i.e. trace, positive, negative) results are documented in INPC. There may be other reasons at the institutional level, such as that some routine results are not sent to INPC due to



administrative burden or cost. It is recommended that the usability and utility of a post-donation UA to improve understanding of live donor risk as supported by the current OPTN/UNOS Living Donor Follow-Up Worksheet (Appendix C) and affiliated regulations, be critically re-examined in future studies. Some the time, both albumin and creatinine are measured in a random urine sample and an albumin/creatinine ratio (ACR) is calculated to more accurately assess kidney function. An ACR may be done to more accurately determine how much albumin is escaping from the kidneys into the urine. This study did not assess ACR.

## Conclusion

This is the first study to examine LKD follow-up at Indiana University Health and reinforces the idea that the capacity to acquire LKD follow-up is affected in part by structures and processes within a health care system. This study provides previously unknown information about historical trends and differences in LKD follow-up care by age and race, where the most significant differences on receipt of 24-month follow-up was age. This knowledge of age-related differences in LKD follow-up care patterns at the transplant center level can assist research teams in the design and development of interventions to improve care and patient outcomes. New population health management tools for LKDs could include administrative and managerial dashboards at the transplant center level. At the patient level, web-based or mobile applications or text messaging could be used to facilitate and sustain communication with younger donors who may be less likely to access the follow-up care.

INPC data demonstrates the ability to capture 24-month follow-up SCr and UA kidney laboratory data. Thus, a statewide HIE, such as demonstrated by INPC, can serve as a catalyst for connecting all hospitals and physicians in a single community, region or state, to provide LKD follow-up data. Further research on access to existing data sources including other existing statewide HIE infrastructures could improve follow-up reporting and compliance as required by OPTN/UNOS for other transplant centers. The transplant community at large may benefit from examining HIE as a new clinical data source for integrating existing data to improve follow-up care for all living donors.

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CHAPTER FIVE: FOLLOW-UP HEALTH OUTCOMES OF LIVING KIDNEY  
DONORS IN A HEALTH INFORMATION EXCHANGE: RENAL FUNCTION,  
DIABETES MELLITUS AND HYPERTENSION

Abstract

Objective: To evaluate the 24-month follow-up health outcomes in living kidney donors (LKDs) including renal function and differences by age, race, and sex as well as incidence of (DM) and hypertension (HTN).

Design: A retrospective cohort study using data from the Indiana Network for Patient Care (INPC).

Participants: Medical records of 392 LKDs aged 19 - 66 years old who donated a kidney between 1999 and 2014.

Methods: Predictors of LKD 24-month renal function including age, race and sex were assessed by linear regression with inclusion of two-way interaction to test for effect modification. Renal function was measured by estimated glomerular filtration rate (eGFR) and was calculated from the mean 24-month follow-up serum creatinine (SCr) measurement using the CKD-EPI equation. Incidence rates of diabetes mellitus (DM) and hypertension (HTN) were identified by administrative diagnosis codes using the International Classification of Disease Modification Ninth Revision Clinical Modification (ICD-9-CM).

Results: Median (IQR) eGFR was 64.8 (18.1) ml/min/1.73m<sup>2</sup>. In the adjusted multiple linear regression model, Black or African-American LKDs had lower follow-up eGFR at 24-months (-7.0 mL/min/1.73m<sup>2</sup>; p=0.008) than those non-Black or African-American.

Male LKDs had lower eGFR ( $-48.5 \text{ mL/min/1.73m}^2$ ;  $p = 0.000$ ) than females. When interactions were introduced into the model, the association was amplified in younger donors and attenuated in older donors ( $0.34 \text{ mL/min/1.73m}^2$ ;  $p = 0.017$ ). One donor had a diagnosis of DM, while three had a HTN diagnosis between one day and  $\geq 24$ -months post-donation.

Conclusions: Post-donation renal function is lower in male and Black or African-American LKDs than females, particularly among younger donors.

Keywords: health information exchange; living kidney donors; chronic diseases; diabetes; hypertension

## Introduction

Follow-up for living kidney donors (LKDs) in the first 24-months (or two-years) following donation are important processes of care in order to monitor post-surgical complications, to ensure patient safety, and to provide informed consent for future donor candidates. Since 2013, during the 24-month follow-up period mandated by the Organ Procurement and Transplantation Network (OPTN), transplant centers are required to report health outcomes of interest including renal function via kidney laboratory data, and the development of diabetes mellitus (DM) and hypertension (HTN) from laboratory data collected on the LKD. (OPTN, 2016b). As part of OPTN informed consent policy, candidates undergoing evaluation must be informed that they may have a 25-35% permanent loss in kidney function after donation (OPTN, 2016b). This is because kidney donation can lead to a loss of approximately 50% of nephron mass, with an immediate and corresponding decrease in renal function; however, the remaining healthy renal parenchyma has the ability to recover a significant percentage of lost function within a relatively short time (Srinivas & Poggio, 2012). As a measure of renal function, a glomerular filtration rate (GFR) can be calculated from serum creatinine (SCr) based formulas. Furthermore, an estimated glomerular filtration rate (eGFR) measurement is a closer estimate of true GFR than serum creatinine alone and is recommended for use in clinical practice by many authorities (A. S. Levey et al., 1999; A. S. Levey et al., 2003; A. S. Levey et al., 2005).

Kidney Disease Improving Global Outcomes (KDIGO) calls CKD a global public health problem, and there are approximately 13% of American adults with the disease (Coresh et al., 2007; Drey, Roderick, Mullee, & Rogerson, 2003; A. Levey et al.,



2007; A. S. Levey & Coresh, 2012; A. S. Levey et al., 2011). As shown in Table 5.1, in Stage 1, renal function remains normal and then becomes minimally reduced in Stage 2. According to the National Institute of Diabetes, Digestive and Kidney Diseases, a GFR of 60 mL/min per 1.73 m<sup>2</sup> or higher is the normal range, while numbers below 60 may indicate CKD. Pre-donation GFR values exceeding 80 mL/min per 1.73 m<sup>2</sup> are usually considered suitable for living kidney donation, but guidelines are not specific the method on how GFR should be calculated (OPTN, 2016c). Nevertheless, no standardized reference values exist for many of the procedures used to assess renal function used in clinical practice and thus, the decision of proceeding (or not) with donation is unfortunately often a matter of subjective interpretation rather than more precise science.(Srinivas & Poggio, 2012). As there is a significant emphasis placed by the NKF on GFR to determine the state of renal health versus disease, renal function assumes an even greater role in understanding living donor outcomes (A. S. Levey et al., 2003).

**Table 5.1 The Five Stages of Chronic Kidney Disease**

Stage	Qualitative Description	GFR
<b>1</b>	Normal or high GFR	> 90 mL/min
<b>2</b>	Mild CKD	60-89 mL/min
<b>3A</b>	Moderate CKD	45-59 mL/min
<b>3B</b>	Moderate CKD	30-44 mL/min
<b>4</b>	Severe CKD	15-29 mL/min
<b>5</b>	ESRD	<15 mL/min

Source: The National Kidney Foundation

GFR = glomerular filtration rate, CKD = chronic kidney disease

Normal GFR results range from 90 - 120 mL/min/1.73 m<sup>2</sup>

Most people will not know they have Stage 1 CKD, unless discovered during screening for another condition, including testing for DM and HTN. As two of the leading causes of CKD, DM and HTN historically have been contraindications to living kidney donation and exclude a candidate early in the evaluation and screening phase (Chen et al., 2004; Pyram, Kansara, Banerji, & Loney-Hutchinson, 2012). Although few transplant centers will approve LKD candidates with impaired glucose tolerance, most, if not all, have historically denied candidates with a diagnosis of DM (Bia et al., 1995; D. Mandelbrot et al., 2007; Vigneault, Asch, Dahl, & Bia, 2011). Currently, OPTN policy lists DM as absolute *exclusion* criteria for living kidney donation (OPTN, 2016c). Although the clinical definition of HTN has changed over time with different levels of acceptable diagnosis and treatment thresholds (Carretero & Oparil, 2000) individuals diagnosed and untreated have commonly been excluded from donating a kidney in the past on the basis that nephrectomy may increase blood pressure (Ierino, Boudville, & Kanellis, 2010).

Addressing follow-up clinical outcomes in LKDs including those of DM and HTN is becoming easier as new clinical data sources such as health information exchange (HIE) have increasingly captured follow-up kidney laboratory data. There is now an opportunity to improve knowledge about follow-up health outcomes for this newly identified cohort of LKDs. The objective of this study is to examine follow-up health outcomes including renal function and differences in age, race and sex, and to describe the incidence of DM and HTN in a cohort of LKDs at 24-months post-donation follow-up.

## Methods

### *Data Source*

The Indiana Network for Patient Care (INPC) is the database of clinical and other information that is available through the Indiana Health Information Exchange. Derived from a variety of Electronic Health Record (EHR) systems, INPC represents one of the largest patient networks in the country (Biondich & Grannis, 2004). Over 100 separate healthcare entities provide data to INPC including: major hospitals, health networks, and insurance providers. INPC also includes outpatient data from participating physician offices, community health and indigent care centers, county and state public health departments, national laboratories, payers and ancillary sources such as radiology systems (Biondich & Grannis, 2004; McDonald et al., 2005). When combined, the information from these institutions represent data on over 17 million patients in the form of 4.9 billion clinical observations, 951 million encounter records and over 195 million multimedia reports (Institute, 2015).

### *Participants*

Three hundred ninety-two LKDs (N = 392) who donated a kidney between January 1999 and May 2014 at Indiana University Health who received follow-up care at 24-months post-donation, make up the sample population for this study (See Chapters 3 - 4). All LKDs in this study are believed to have timely and complete follow-up as measured by the  $\pm 60$  days of the 24-month anniversary of the donation date.

### *Outcome Measures*

Appendix D contains a detailed supplemental literature review about the selected outcome and predictor variables used in previous studies of LKDs.

**Renal function measured by (eGFR)** was calculated from the serum creatinine (SCr) value reported  $\pm 60$  days of the 24-month anniversary of the donation date using the CKD-EPI equation:  $GFR = 141 * \min(SCr/\kappa, 1)^\alpha * \max(SCr/\kappa, 1)^{-1.209} * 0.993^{Age} * 1.018 [\text{if female}] * 1.159 [\text{if black}]$ . SCr is serum creatinine (mg/dL),  $\kappa$  is 0.7 for females and 0.9 for males,  $\alpha$  is -0.329 for females and -0.411 for males, min indicates the minimum of SCr/ $\kappa$  or 1, and max indicates the maximum of SCr/ $\kappa$  or 1. If there were multiple 24-month SCr values in INPC for the donor, the mean was used. The CKD-EPI equation calculates eGFR based on sex as a binary variable (Male or Female), race as a binary variable (Not Black or African-American, or Black or African-American), current age in years as a continuous variable, and SCr in mg/dL (Florkowski & Chew-Harris, 2011). Note: The race variable used for eGFR was computed where non-Black or African-American included Asian, Native American Pacific Islander, or White LKDs. If race was classified in INPC as ‘null or code not mapped’ and ‘other or unknown’ the LKD was treated as missing data and were therefore was not included in analysis of eGFR.

**Diabetes mellitus (DM):** Diagnosis of DM was determined based on International Classification of Disease Ninth Revision Clinical Modification (ICD-9-CM) code 250 or an internal diagnosis code (DM, non- insulin dependent, DM uncontrolled, diabetes out of control, diabetic, DM) used by the healthcare provider or system and accessible within INPC to the experienced data analyst at Regenstrief Institute. DM diagnosis was

classified if the diagnosis code appeared in INPC  $\geq$  one day but within  $\leq$  790 days (24-months after the kidney donation  $\pm 60$  days).

**Hypertension (HTN):** Diagnosis of HTN was based on ICD-9-CM codes including 401.0 malignant essential HTN, 401.1 benign essential HTN, 401.9 unspecified essential HTN, 405.01, malignant renovascular HTN, 405.09, other malignant secondary HTN, 405.11, benign renovascular HTN, 405.19 other benign secondary HTN, 405.91 unspecified renovascular HTN, and 405.99 other unspecified secondary HTN. HTN diagnosis was determined if the diagnosis code appeared in INPC  $\geq$  one day but within  $\leq$  790 days (24-months after the kidney donation  $\pm 60$  days).

#### *Independent Variables*

**Age at time of donation** has a normal distribution and was treated as a continuous variable.

**Race** was treated a binary categorical variable classified as non-black or African-American (0) and Black, African-American (1).

**Sex** was a binary variable and defined as female (0) and male (1).

Note: The race variable used for eGFR was computed where non-Black or African-American included those with races in INPC classified as Asian, Native American Pacific Islander, or White. If race was classified in INPC as ‘null or code not mapped’ and ‘other or unknown’ the subject was treated as missing data and were therefore not included in analysis of eGFR.

#### *Statistical Analysis*

Predictors of follow-up eGFR at 24-months including age, race and sex were

assessed with multiple linear regression and the inclusion of two-way interaction to test for effect modification. Incidence proportion and rate for new cases of post-donation DM and HTN at 24-month donation anniversary (+ 60 days) was calculated. All analyses and descriptive statistics were carried out with SPSS, version 23 (IBM SPSS Statistics, Inc.) with a 95% confidence level where  $p (<0.05)$  is considered significant.

## Results

Of 392 LKDs that received follow-up at 24-months, the median interquartile range (IQR) age at time of donation was 41 years old (33-51). Two hundred and thirty-two (61.7%) LKDs were female and 150 (38.3%) were male. Thirty-six (9.2%) LKDs were Black or African-American. For analysis of follow-up renal function at 24-months (eGFR CKD-EPI), there were 386 LKDs included. Follow-up renal function at 24-months by LKD baseline demographic characteristics are presented in Table 5.2 (*Note: baseline demographics as presented in tabular form show age as a categorical variable; age was used as a continuous variable in all reported analyses*). The median age at time of donation was 40.4 years. Median 24-month post-donation eGFR was 62.8, while the mean eGFR was 64.8 (S.D.=15.5, 95% CI 63.2 - 66.3) mL/min/1.73m<sup>2</sup>.

The multiple linear regression model presented in Table 5.3 accounted for 61.7% of the variance in eGFR,  $F(4,381) = 155.82$ ,  $p < 0.000$ . Sex makes the strongest contribution to explaining the dependent variable eGFR ( $p = 0.000$ ). In the adjusted model, Black or African-American LKDs had lower post-donation eGFR (-7.0 mL/min/1.73m<sup>2</sup>;  $p=0.008$ ) than those non-Black or African-American. Male LKDs had lower eGFR (-48.5 mL/min/1.73m<sup>2</sup>;  $p = 0.000$ ) than females at 24-month follow-up. When interactions were introduced into the model, the association of moderating

variables age and sex was amplified in younger donors and attenuated in older donors (0.34 mL/min/1.73m<sup>2</sup>;  $p = 0.017$ ).

The incidence proportion of DM at 24-months is one in 392, and for HTN is three in 392; the incidence rates are 0.25% and 0.77% respectively. With such few disease outcomes, further and additional inferential statistical analysis could not be reported for this study.

**Table 5.2 Non-Adjusted Post-Donation Living Kidney Donor Renal Function at 24-Months by Baseline Donor Demographics**

	Median eGFR <sup>a</sup>	Mean eGFR	Standard Deviation	Lower CL 95%	Upper CL 95%
<b>Age Category</b>					
<i>19-39</i>	88.9	93.5	25.4	89.7	97.3
<i>40-49</i>	84.9	83.4	21.4	79.2	87.6
<i>50-59</i>	68.1	70.7	19.6	66.5	74.9
<i>60+</i>	79.5	75.6	17.0	68.3	82.9
<b>Race</b>					
<i>Non-Black African- American</i>	83.3	85.3	24.5	82.7	87.9
<i>Black or African- American</i>	80.3	78.7	23.8	70.7	86.7
<b>Sex</b>					
<i>Male</i>	92.9	96.8	21.3	94.1	99.5
<i>Female</i>	64.7	65.2	14.5	62.8	67.5

Source: 1999-2014 Indiana Network for Patient Care

Notes:  $N = 386$

a. eGFR = Estimated Glomerular Filtration Rate is expressed as mL/min/1.73m<sup>2</sup> as calculated by CKD-EPI equation where expressed as a single equation, is:  $GFR = 141 * \min(SCr/\kappa, 1)^\alpha * \max(SCr/\kappa, 1)^{-1.209} * 0.993^{Age} * 1.018$  [if female]  $* 1.159$  [if black] where SCr is serum creatinine (mg/dL),  $\kappa$  is 0.7 for females and 0.9 for males,  $\alpha$  is -0.329 for females and -0.411 for males, min indicates the minimum of SCr/ $\kappa$  or 1, and max indicates the maximum of SCr/ $\kappa$  or 1.

CL = Confidence limit. The 95% confidence limits are calculated as  $\beta \pm (1.96 \times \text{standard error})$

**Table 5.3 Results of Linear Regression of Post-Donation Renal Function at 24-Months by Age, Race, and Sex, Living Kidney Donors**

Variable	Coefficient ( $\beta_k$ )	Standard error	<i>t</i> -statistic	<i>P</i> -value	Lower 95% CL	Upper 95% CL
Age	-1.14 <sup>b</sup>	0.09	-13.12	0.000*	-1.31	-0.97
Race	-7.04	2.66	-2.65	0.008*	-12.3	-1.8
Sex	-48.53	6.39	-7.59	0.000*	-61.1	-35.95
Age/Sex Interaction	0.34	0.14	2.60	0.017*	0.062	0.624

Source: 1999-2014 Indiana Network for Patient Care

Notes:  $N = 386$  *F*-Statistic is 155.822 with 4 df; adjusted  $R^2 = 0.617$

Coefficients are for Estimated Glomerular Filtration Rate (eGFR) and presented as unstandardized CL = Confidence limit. The 95% confidence limits are calculated as  $\beta \pm (1.96 \times \text{standard error})$ , with a *P*-value  $< 0.05$  considered to be significant\*

## Discussion

The goal of the present study was to understand differences in post-donation eGFR and the incidence of DM and HTN at the time of 24-month follow-up in a newly identified retrospective cohort of LKDs. Results of an adjusted linear regression model shows that eGFR was lower in black and male LKDs with the association amplified in younger donors at the 24-month follow-up. Age is a known natural predictor of renal function decline in health adults (Epstein, 1996; Lindeman, Tobin, & Shock, 1985; Lindeman, Tobin, & Shock, 1984). In LKDs, renal function of the remaining kidney is expected to improve for many years, but will show signs of slight deterioration long-term ( $>15$  years) (Fehrman-Ekholm et al., 2011). The identification of the risk of post-



donation renal decline resulting in CKD is limited to the first year post-donation in most studies; However, previous studies have clearly shown that a variable fraction of LKDs will have eGFR values  $<60 \text{ mL/min/1.73 m}^2$  and that the risk of such post-donation CKD varies with age at time of donation, baseline eGFR, and demographics such as sex and race (Barri, Parker III, Kaplan, & Glasscock, 2009; A. Garg et al., 2006; Najarian, McHugh, Matas, & Chavers, 1992; Parasuraman & Venkat, 2008; Poggio et al., 2009; Wan, Spalding, Winch, Brown, & Geddes, 2007). The unadjusted median eGFR measurements for our cohort ranged from  $68.1 \text{ mL/min/1.73 m}^2$  to  $88.9 \text{ mL/min/1.73 m}^2$ . These results are consistent with what is disclosed in the OPTN/UNOS informed consent process, and places the LKDs in this cohort within the CKD spectrum as outlined by the National Kidney Foundation.

Renal diseases typically begin in middle age and take decades to progress to from CKD to ESRD at a median age of 64, therefore, existing 10-15 year studies will not capture the lifetime risks of post-donation ESRD (Grams, Chow, Segev, & Coresh, 2013). Most renal diseases will cause lesser decreases in renal function beginning in middle age, while the prevalence of a  $\text{GFR} < 30 \text{ mL/min/1.73 m}^2$  increases sevenfold from ages 40 to 50, and increases again almost threefold to about 1% of the population by age 60 (Grams et al., 2013; Hoerger et al., 2010). Therefore, while ESRD was not assessed in this study, data shows that younger LKDs are at demonstrably higher risk than older candidates for developing ESRD (Steiner, 2014) as there is only a 2-3% lifetime risk for ESRD that manifests from ages 30-40, while at age 60 more than half the lifetime risk for ESRD remains (Narayan, Boyle, Thompson, Sorensen, & Williamson, 2003). Therefore,

the progression of CKD to ESRD in LKDs is a valid concern in the transplant community.

New research assessing the incidence of HTN and DM in a national cohort of LKDs found that the risk of ESRD secondary to diabetes and hypertension was low in early years post-donation and increased substantially over time (Anjum et al., 2016). The development of a chronic condition post-donation such as DM and HTN would put an LKD at increased risk for CKD and ESRD. As with all else equal, if kidney donation sacrificed  $40 \text{ mL/min/1.73 m}^2$ , because of the development of post-donation diabetic nephropathy or other diseases that lost an additional  $40 \text{ mL/min/1.73 m}^2$  per decade, an individual would reach ESRD ten years earlier because of donation (Keith, Nichols, Gullion, Brown, & Smith, 2004; Steiner, Ix, Rifkin, & Gert, 2014).

In this current study, one LKD developed DM and three (0.07%) developed HTN by the time of 24-month follow-up. In a systematic review of the literature from 1966 to 2006, Young et al. noted that living donors studied up to 11 years post-donation seldom develop the metabolic, endocrine, hematology or micro-inflammatory disturbances commonly associated with established CKD caused by parenchymal renal disease leading to ESRD (Young et al., 2007). However, according to the United States Renal Data Service, Type 2 DM causes almost all acquired, adult onset ESRD, with an overall lifetime risk of self-reported diabetes risk of 33% in men and 39% in women that is increased to about 50% for Hispanic and Black or African-American women (Narayan et al., 2003). This is increasingly important with new targeted educational interventions for minority populations (Gordon et al., 2015), as well as several other interventions designed with the goal of educating transplant centers and patients on strategies that can

be implemented to assist in reducing disincentives for transplant candidates in seeking living donation (Boulware et al., 2011; Patzer et al., 2015; J. Rodrigue, Cornell, Lin, Kaplan, & Howard, 2007; J. R. Rodrigue et al., 2015; Amy D Waterman et al., 2015).

While Type 2 DM is not common in individuals under 30 years old, current protocols used by transplant centers to screen and exclude living donor candidates have not reduced the risk of post-donation diabetes (Boyarsky BJ, 2012; H. N. Ibrahim et al., 2009; Lentine et al., 2010). There are a number of older studies that report incidence rates of HTN following kidney donation at various follow-up points, ranging between 9% and 48% (Anderson et al., 1985; Dunn et al., 1986; Fehrman-Ekholm et al., 2011; Hakim, Goldszer, & Brenner, 1984; Miller et al., 1985; Talseth et al., 1986; Tapson et al., 1985; Torres et al., 1987; Warnick, Jenkins, Baumgarten, & Bia, 1988). Another study showed that Black or African-American race is associated with an increased risk for the development of post-donation HTN as compared to white donors (Doshi, Goggins, Li, & Garg, 2013; Lentine et al., 2010). Assessing risk for HTN attributable to kidney donation has been challenging and very few studies have done such that would be included for evidence in clinical guideline development (See Appendix D). A more recent retrospective matched-control cohort of 1,200 LKDs assessing post-donation HTN with a mean follow-up of 6.4 years, found that LKDs had a 40% increased risk (hazard ratio, 1.4; CI, 1.2–1.7) of being diagnosed with HTN compared with that of non-donor controls (A. X. Garg et al., 2008). In another study, HTN increased from 14% in the early post-donation period to 57% in the late post-donation period, however, the sample size was small (n=21) and the extent to which incident HTN is attributable to kidney donation is difficult to judge (Lenihan et al., 2015). While this study did not assess blood pressure,

recently a prospective study of LKDs and matched healthy controls found no difference in blood pressure between LKDs and controls observed for the first three years after donation (Kasiske et al., 2015).

There are several limitations to this study that deserve mention. First, we are only assessing outcomes for LKDs that are known to have received follow-up care at 24-months post-donation based on kidney laboratory data (See Chapter 4). We do not have mortality data on these LKDs to date in INPC. Additionally, analysis of renal function with eGFR (CKD-EPI) is acceptable in CKD epidemiology and clinically; however there is the possibility that different calculations for eGFR such as the Modification of Diet in Renal Disease Study would provide different results (Matsushita et al., 2012).

Assessment of pre and post-donation renal function are critical aspects of the evaluation and follow-up care process, and the obtained information should always be interpreted in the context of other clinical and laboratory data were not assessed in this study. We used the threshold of +60 days from the 24-month donation anniversary to assess incidence of DM and HTN, which were identified only by ICD-9-CM codes captured within INPC. Therefore, there could be LKDs who received follow-up care at 24-months in our sample who developed DM or HTN, but a diagnosis was not captured by INPC. Due to such few DM and HTN outcomes at 24-months post-donation, inferential analyses would result in insignificant findings and reporting these cases could compromise patient confidentiality.

The present study begins to advance the state of knowledge about health outcomes in a cohort of LKDs from Indiana University Health, including renal function measured as eGFR and the development the chronic conditions DM and HTN during the 24-month follow-up period currently mandated by the OPTN. At the transplant center

level, this knowledge can be used to support LKD candidate education, screening, and informed consent.

## Conclusion

Follow-up health outcomes from this cohort of LKDs identified in a statewide HIE demonstrate that 24-month renal function is lower in male and black or African-American LKDs. Only one donor developed DM and three developed HTN by 24-month follow-up. Knowledge of follow-up health outcomes in this cohort can be useful at the transplant center level and to the larger scientific community in better understanding and promoting improved informed consent for living donation based on the most current CKD epidemiology. Future research should evaluate these findings in larger samples of LKDs in order to assess risk of DM and HTN attributable to living kidney donation.

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## CHAPTER SIX: CONCLUSIONS AND FUTURE RESEARCH

Follow-up care is critical for understanding health outcomes of LKDs, but historically many have been lost-to-follow-up in the months and years following donation. This chapter addresses how each study in this dissertation makes a scientific contribution to our better understanding of living donor health outcomes and provides practice and policy implications and future research steps.

The transplant community has now recognized that despite past and current efforts to increase registrations for organ donation, the number of deceased donors will never be sufficient (Goldberg, French, Abt, & Gilroy, 2015). Living donor kidney transplants have better graft survival rates than transplants with deceased donor kidneys, significantly reduce the national waiting list, allow for incompatible kidney paired donation, and allow preemptive renal transplantation prior to dialysis for end-stage renal disease (ESRD) (Matas et al., 2015; A. D. Waterman et al., 2015). Patient safety remains at the foundation of clinical and ethical discussions regarding the practice of living donation.

### Clinical Informatics to Identify Living Kidney Donors in Novel Clinical Data Sources

In this dissertation, a novel method for identifying LKDs in a statewide Health Information Exchange (HIE) was applied using a novel text-mining approach and tools of clinical informatics including natural language processing (See Chapter 3). To our knowledge, this study is the first of its kind to identify LKDs in HIE. The LKD cohort identified showed high correlation with Organ Procurement and Transplantation Network LKD frequency by year ( $r = 0.948$ ), demonstrating that the methodology was effective



for our sample population. As HIE efforts expand across the nation, these repositories are valuable sources that be further explored for use in clinical and research scenarios to improve follow-up and involving patients who span many care providers. The introduction of new big data sources like HIE which have the capacity to capture laboratory data over time may very well contribute to our knowledge of live donor outcomes. This dissertation demonstrated that the tools of clinical informatics assist in identifying and to study follow-up outcomes of living kidney donors (LKDS) in novel clinical data sources.

#### Big Data and Statewide Health Information Exchange to Evaluate Living Kidney Donor Follow-Up Care Patterns

Transplant centers must submit living donor follow-up data for two-years (24-months) from the anniversary of the kidney donation. As explored in Chapter 4 of this dissertation, the Indiana HIE demonstrates the capacity to capture follow-up kidney laboratory data on the cohort of identified LKDs. LKDs between the ages of 40 – 49 have are 1.3 times more likely of having 24-month follow-up, while those aged 50 – 59 are 1.8 times more likely as compared to 19-39 year olds. LKDs in the third donor era (2009-2012) were 65.1 times more likely to have 24-month follow-up than those who donated before 2004 while those LKDs in the fourth era (2013-2014) were 22.2 times more likely than those donating between 1998 and 2004 to receive 24-month follow-up ( $p = 0.000$ ). Black or African-American LKDs were about twice as likely than those non-black or African-Americans to have 24-month follow-up ( $p = 0.014$ ).

This study shows that while 24-month follow-up has improved over time, younger LKDs under 40 may be less likely to get follow-up care than those in older age categories. In addition to differences in receipt of follow-up care by age and other predictors; follow-up care patterns reflect the development of new policy by the Organ Procurement and Transplantation Network/United Network for Organ Sharing (OPTN/UNOS) Living Donor Committee extending follow-up requirements.

#### Examining Health Outcomes of Living Kidney Donors in a Health Information Exchange

In this study the 24-month follow-up health outcomes in living kidney donors (LKDs) including renal function and differences by age, race, and sex as well as incidence of (DM) and hypertension (HTN) were evaluated. Predictors of LKD 24-month renal function including age, race and sex were assessed by linear regression with inclusion of two-way interaction to test for effect modification. Renal function was measured by estimated glomerular filtration rate (eGFR) and was calculated from the mean 24-month follow-up serum creatinine (SCr) measurement using the CKD-EPI equation. Incidence rates of diabetes mellitus (DM) and hypertension (HTN) were identified by administrative diagnosis codes using the International Classification of Disease Modification Ninth Revision Clinical Modification (ICD-9-CM).

Median (IQR) eGFR was 64.8 (18.1) ml/min/1.73m<sup>2</sup>. In the adjusted multiple linear regression model, Black or African-American LKDs had lower follow-up eGFR at 24-months (-7.0 mL/min/1.73m<sup>2</sup>; p=0.008) than those non-Black or African-American. Male LKDs had lower eGFR (-48.5 mL/min/1.73m<sup>2</sup>; p = 0.017) than females. When interactions were introduced into the model, the association was amplified in younger

donors and attenuated in older donors ( $0.34 \text{ mL/min/1.73m}^2$ ;  $p = 0.017$ ). One donor had a diagnosis of DM, while three had a HTN diagnosis between one day and  $\geq 24$ -months post-donation. Post-donation renal function is lower in male and Black or African-American LKDs than females, particularly among younger donors.

While this study only assessed LKD outcomes at 24-month follow-up, there should be no controversy that a continued commitment to increasing knowledge about long-term health outcomes ( $>2$  years; See Chapter 2, Henderson Conceptual Model for Living Kidney Donor Follow-up) is essential to ensure patient safety in living kidney donation. This is particularly true as new-onset morbidity including the development of diabetes and hypertension takes years to emerge, making it highly likely that they will be missed during the 24-month (two-year) follow-up period currently mandated by OPTN, the United Network for Organ Sharing (UNOS), and the Centers for Medicare and Medicaid Services. It is known that kidney function declines with time, and there are data showing a minority of LKDs progressing to chronic kidney disease (CKD), with some even requiring dialysis (Gibney, Parikh, & Garg, 2008; Klop et al., 2015; Nazarian & Reese, 2015; P. P. Reese, Boudville, & Garg, 2015; Ross, 2015). The data also are clear in demonstrating that when LKD renal function declines, it occurs more than 5 to 7 years after the nephrectomy (Muzaale et al., 2014).

## Practice and Policy Considerations

It has been an ongoing challenge in the United States to enact policies requiring a comprehensive long-term assessment of living donor health. After two years, follow-up reporting is no longer required by OPTN/UNOS (OPTN, 2013) and the living donor is left to primary care for lifetime follow-up care. With only a short-term assessment required post-donation, living donors may go years without any preventive and primary health care services. The intent of a longer UNOS/OPTN living donor follow-up policy, including regular and routine monitoring including laboratory testing which could be established, the progression of renal function decay could be delayed or stopped. While it is recognized that the current OPTN/UNOS living donor follow-up policies were created and implemented with much comprise from the transplant community, health policy that dictates long-term follow-up for the donors would be advantageous. A policy that required longer than two-year follow-up would allow for a more timely recognition of the living donors at greater risk of developing post-donation renal failure. Furthermore, a long-term living donor follow-up policy would allow the collection of the biological and medical data of all donors beyond two years. This would help to better predict long-term outcomes post-donation and would support selection of living donor candidates with the best-predicted outcome.

As short-term (24-month) follow-up is difficult to achieve at the transplant center level and the complexity of long-term data collection (outside of established HIE as discussed in this dissertation) has been documented from the transplant center perspective (Amy D Waterman et al., 2013). Commonly, patient-level barriers are reported, noting that the donor is unable to return to the transplant center, that the contact information is

outdated, or that the donor does not want to be contacted. Most importantly and from a patient-centered perspective, there is currently a lack of reimbursement to the donor's costs associated with follow-up. We know that indirect and direct post expenses vary increasingly by distance traveled to the transplant center (J. Rodrigue et al., 2016). Health system-level barriers such as the lack of reimbursement to programs to cover the cost of living donor follow-up, additional medical and laboratory testing, and staff time were also reported by OPTN member transplant programs surveyed (A. D. Waterman et al., 2013).

Improvements in follow-up may occur if transplant programs work with donors to develop plans to achieve follow-up, if programmatic standards are set for completeness in follow-up data reporting, and if sufficient staff resources are available to ensure ongoing post-donation contact. This acknowledges that the responsibility for lack of follow-up cannot be borne only by the transplant system. The patients themselves need incentives to continue to follow-up, either with the transplant center or with their primary care provider (PCP). Transplant centers, OPTN/UNOS policy, and current practice recommendations support the idea of living donor follow-up in primary care settings (Leichtman et al., 2011). With the documented barriers of follow-up from the transplant center perspective (Amy D Waterman et al., 2013), primary care is an ideal care environment for the management of corrective and preventive clinical measures, including lifestyle modifications that could mitigate the progression of chronic disease leading to renal decline.

Placing LKD follow-up within the context of primary care eliminates potential conflicts of interest with transplant providers. The LKD normally has no connection with

the transplant physicians aside from the surgery, and there is evidence showing that transplant physicians are more likely to report that living donor health is good, making the argument that follow-up is not needed (D. A. Mandelbrot & Pavlakis, 2012).

Theoretically, PCPs can conduct all aspects of the annual follow-up and then deliver the results to OPTN/UNOS, where the LKD is already known via living donor registration and follow-up forms. The detection of declining renal function through laboratory tests such as serum creatinine and urine protein screening tests should prompt referral to a nephrologist. Currently there is no formal education directed towards PCPs that provide clinical practice recommendations for the post-donation care and lifetime management of LKDs. This educational guidance could be a new project considered by the OPTN/UNOS Living Donor Committee in the future.

The Henderson Conceptual Framework for Living Kidney Donor Follow-Up supports the theory that structures and processes of care impact outcomes of care. Proposals to improve and to enhance the quality of LKD follow-up must acknowledge the two structural elements of care including the U.S. organ transplant system and the individual transplant center that is responsible for the timely and complete reporting. There are both internal and external processes of LKD follow-up care, including care provided at the individual transplant center and care that is expected long-term in primary care settings. Outcomes of these care processes result in both short-term and long-term collection of clinical data on living donor health and wellbeing.

## Future Research

### *Formal Validation of Text-Mining Algorithm*

This dissertation advances towards our understanding of HIE as a new source for evaluating health outcomes in LKDs. In addition, the protocol for the identification of LKDs within the HIE presents a new approach to capturing and extracting data in transplantation research. As a preliminary step to this study, I will have the ability to formally validate the text-mining terms used to identify LKDs for the Indiana University Health cohort (See Chapter 3 for a brief description of the methodology) in the Johns Hopkins comprehensive Electronic Medical Record (EMR) system that contains records of all past LKDs who donated at the center.

### *Future Research on Indiana University Health Cohort*

Future research on the cohort LKDs from Indiana University Health includes the study of longitudinal clinical health outcomes beyond the short-term follow-up period. In addition, future studies will include: an examination of post-donation hospitalizations; incidence of DM and HTN in the long-term follow-up period, diabetes control based on a glycosylated hemoglobin (HbA1C), anti-diabetic and anti-hypertensive medication use in those LKDs; and; LKD renal function (eGFR) trajectory based on pre-donation renal function data.

### *A Text-Mining Approach to Understanding Sequelae of Live Donation*

Dorry Segev, MD, PhD, Professor of Surgery and Associate Vice Chair for Research, Department of Surgery, Johns Hopkins School of Medicine, has applied for a supplemental research award to the National Institute for Diabetes, Digestive, and Kidney Diseases (NIDDK) to provide me with protected time, training, and mentoring related to

conducting research focused on understanding live kidney donor risk. My goal is to become an independent investigator committed to improving clinical outcomes and quality of life for live kidney donors. My research proposal to the NIDDK aims to better understand the long-term sequelae of living kidney donation for LKDs, such as risk of developing post-donation conditions through a text-mining approach of medical records. Beyond structured data fields traditionally found in EMRs, unstructured clinically useful information can be found in plain text clinical and narrative notes (Raghupathi & Raghupathi, 2014). However, this information must often be manually ascertained and extracted from an EMR, which is a time-consuming and expensive process.

#### *Understanding Diabetes and Living Donation*

One example of information that is time-consuming to collect from an EMR is fasting blood glucose (FBG); structured data may contain laboratory values for serum glucose, but whether the sample was taken after fasting is unknown. Iterative text mining approaches and machine learning algorithms such as natural language processing (NLP) and have been used to identify procedures and to derive comorbidities and results from plain text reports in other clinical settings (Carrell et al., 2014; Martinell, Stålhammar, & Hallqvist, 2012; Salmasian, Freedberg, & Friedman, 2013; Wieneke et al., 2015) and to quantify association between diseases, conditions, and symptoms (Bassøe, 1995; Lee, Wu, & Yang, 2007; Meystre, Savova, Kipper-Schuler, & Hurdle, 2008; Roque et al., 2011; Xiaoyan Wang & Amy Chused, 2008).

As part of the OPTN requirements for screening and evaluation of living kidney donor candidates, FBG is required; donor candidates undergo either a glucose tolerance test or (in the presence of high perceived risk for diabetes, such as family history) a



HbA1C test (OPTN, 2016c). At some centers, HbA1C is tested in all donor candidates, regardless of metabolic risk. Diabetes mellitus (DM), in addition to uncontrollable hypertension or history of hypertension with evidence of end organ damage, is currently an OPTN exclusion criterion for living kidney donation (OPTN, 2016c). However, there was previously more variation in this practice among U.S. transplant centers as older data demonstrated that factors associated with DM in kidney donors are similar to those in the general population and that donors screened carefully at the time of donation do not appear to have disease acceleration (H. Ibrahim et al., 2010; P. Reese et al., 2008). Furthermore, historically protocols used by transplant centers to screen and exclude LKD candidates have not reduced the risk for post-donation diabetes (Boyarsky BJ, 2012; H. N. Ibrahim et al., 2009; Lentine et al., 2010). While a pre-donation FBG laboratory test is required by policy, this characteristic is difficult to extract automatically as recorded in donor medical records.

An understanding of pre-donation FBG and incidence of post-donation diabetes mellitus (DM) may improve our knowledge about the long-term risks and sequelae associated with kidney donation, particularly for younger African-American (AA) donors who may be at higher risk (Steiner et al., 2014). This can improve donor selection processes, informed consent, and post-donation care. To better understand risk for the development of sequelae such as DM in LKDs, we propose an ancillary study within an on-going, R01-funded multicenter cohort of live donors. The parent R01 study is recruiting 4,215 AA live donors at 13 centers using a retrospective design to maximize the duration of long-term follow-up in each participant (since prospective study of donors requires 10-20 years before outcomes are manifest). The parent study conducts patient

interviews and collects longitudinal medical records including the comprehensive pre-donation medical evaluation and all subsequent physician visits during the post-donation period.

The proposed ancillary study leverages prior experience in applying a text mining approach and NLP in the medical setting with an existing multicenter study of LKDs. We propose to develop a novel case-detection algorithm for automatically ascertaining and extracting pre-donation FBG from EMRs of LKDs. We then propose to apply this novel case-detection algorithm to explore the association between pre-donation FBG and risk of post-donation DM. This concept is highly likely to generalize beyond FBG and DM.

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## APPENDICES

## Appendix A: Text-Mining Terms for a Natural Language Processing Case Finding

## Algorithm to Identify Living Kidney Donors in Chapter Three

*Any term in quotes is a search for that exact term; any term in quotes with a note after it “these words found within X words of each other” means that the terms in quotes must all be there, but they could appear in any order, and they can be up to “X” words away from each other.*

- "PRINCIPAL DIAGNOSIS: Living kidney donor" AND "donor nephrectomy"
- "DISCHARGE DIAGNOSIS: Living kidney donor"
- "DISCHARGE DIAGNOSIS: kidney donor"
- "post donor nephrectomy" - these words found within 5 words of each other
- "recent donor nephrectomy" - these words found within 5 words of each other
- "procedure donor nephrectomy" - these words found within 7 words of each other
- "discharge kidney donation" - these words found within 10 words of each other
- "PRINCIPAL DIAGNOSIS kidney donor" - these words found within 10 words of each other
  - AND "procedure donor nephrectomy" - these words found within 10 words of each other
- "living donor nephrectomy" - these words found within 10 words of each other
  - AND NOT "kidney transplant" - these words found within 3 words of each other



- AND NOT "renal transplant" - these words found within 3 words of each other
- AND NOT "kidney transplantation" - these words found within 3 words of each other
- AND NOT allograft
- "history donor nephrectomy" - these words found within 6 words of each other
  - AND NOT preoperative
  - AND NOT pre-op
  - AND NOT pre-op
  - AND NOT transplant
  - AND NOT transplantation
- "history kidney donation" - these words found within 5 words of each other
  - AND NOT preoperative
  - AND NOT pre-op
  - AND NOT preop
  - AND NOT evaluate
  - AND NOT examination
  - AND NOT evaluation
- "PRINCIPAL donor" - these words found within 5 words of each other
  - AND kidney OR nephrectomy OR renal
  - AND living
  - AND NOT "procedure transplant" - these words found within 7 words of each other

- AND NOT "procedures transplant" - these words found within 7 words of each other
- AND NOT "principal transplant" - these words found within 7 words of each other
- AND NOT "kidney transplantation" - these words found within 3 words of each other
- "procedure performed kidney donation" - these words found within 10 words of each other
- "ADMISSION DIAGNOSIS renal donor" - these words found within 3 words of each other
- "DISCHARGE DIAGNOSIS renal donor" - these words found within 3 words of each other
- "ADMISSION DIAGNOSIS: Donor nephrectomy" - these words found within 3 words of each other
- "DISCHARGE DIAGNOSIS: Donor nephrectomy" - these words found within 3 words of each other
- "ADMISSION DIAGNOSIS: kidney donor" - these words found within 3 words of each other
- "DISCHARGE DIAGNOSIS: kidney donor" - these words found within 3 words of each other
- "ADMITTING DIAGNOSIS: Renal donor" - these words found within 3 words of each other

- "PREOPERATIVE DIAGNOSIS: Kidney donor" - these words found within 3 words of each other
- "POSTOPERATIVE DIAGNOSIS: Kidney donor" - these words found within 3 words of each other
- "underwent donor nephrectomy" - these words found within 3 words of each other

And excluded reports with these terms, which were found in reports for *kidney*

*recipients*:

- "Living related donor renal allograft"
- "Successful living related donor renal transplant"
- "kidney rejection"
- "transplant and nephrectomy of that"
- "Renal transplant"
- "History of kidney transplant"
- "related renal transplant"
- "post kidney transplantation"
- "Autotransplant"
- "Autotransplantation"

## Appendix B: Sensitivity Analysis for the Donation Year Variable in Chapter Four

**Model # 1 SCr24**

<b>Variable</b>	<b>Odds Ratio<sup>a</sup> (OR)</b>	<b>P- value<sup>b</sup></b>
<b>Age</b>		
(19-39)		
40-49	1.115	.0496
50-59	1.342	0.093
60+	2.979	0.002*
<b>Race</b>		
(Non-black or African-American)		
Black or African-American	1.439	0.134
<b>Donor Era</b>		
(1998-2003)		
2004-2014	23.972	0.000*

Source: 1998-2014 Indiana Network for Patient Care

Notes: SCr24= Serum Creatinine laboratory follow-up data at 24-months

N = 1,212

a. Odds ratio =  $e^{\log\text{-odds}} = e^{\beta}$ . Also known as relative odds

b. P-values significant at &lt;0.05 are marked \*

**Model # 2 SCr24**

<b>Variable</b>	<b>Odds Ratio<sup>a</sup> (OR)</b>	<b>P- value<sup>b</sup></b>
<b>Age</b>		
(19-39)		
40-49	1.193	0.284
50-59	1.456	0.038*
60+	2.862	0.004*
<b>Race</b>		
(Non-black or African-American)		
Black or African-American	1.503	0.106
<b>Donor Era</b>		
(1998-2004)		
2005-2014	0.041	0.000*

Source: 1998-2014 Indiana Network for Patient Care

Notes: SCr24= Serum Creatinine laboratory follow-up data at 24-months

N = 1,212

a. Odds ratio =  $e^{\log\text{-odds}} = e^{\beta}$ . Also known as relative odds

b. P-values significant at &lt;0.05 are marked \*

**Model #3 SCr24**

<b>Variable</b>	<b>Odds Ratio<sup>a</sup> (OR)</b>	<b>P- value<sup>b</sup></b>
<b>Age</b>		
(19-39)		
40-49	1.275	0.170
50-59	1.596	0.016*
60+	2.609	0.015*
<b>Race</b>		
(Non-black or African-American)		
Black or African-American	1.960	0.013*
<b>Donor Era</b>		
(1998-2003)		
2004-2008	8.535	0.000*
2009-2014	55.949	0.000*

Source: 1998-2014 Indiana Network for Patient Care

Notes: SCr24= Serum Creatinine laboratory follow-up data at 24-months

N = 1,212

SCr24= Serum Creatinine laboratory follow-up data at 24-months

a. Odds ratio =  $e^{\log\text{-odds}} = e^{\beta}$ . Also known as relative odds

b. P-values significant at <0.05 are marked \*

**Model #4 SCr24**

<b>Variable</b>	<b>Odds Ratio<sup>a</sup> (OR)</b>	<b>P- value<sup>b</sup></b>
<b>Age</b>		
(19-39)		
40-49	1.309	0.131
50-59	1.655	0.010*
60+	2.572	0.017*
<b>Race</b>		
(Non-black or African-American)		
Black or African-American	1.961	0.013*
<b>Donor Era</b>		
(1998-2004)		
2005-2008	9.213	0.000*
2009-2014	49.250	0.000*

Source: 1998-2014 Indiana Network for Patient Care

Notes: SCr24= Serum Creatinine laboratory follow-up data at 24-months

N = 1,212

a. Odds ratio =  $e^{\log\text{-odds}} = e^{\beta}$ . Also known as relative odds

b. P-values significant at <0.05 are marked \*

**Note: Model #5 SCr24 was selected for analysis and presentation in the manuscript**

**Model #6 SCr24**

Variable	Odds Ratio <sup>a</sup> (OR)	P- value <sup>b</sup>
<b>Age</b>		
(19-39)		
40-49	1.306	0.139
50-59	1.726	0.006*
60+	3.012	0.006*
<b>Race</b>		
(Non-black or African-American)		
Black or African-American	1.973	0.013*
<b>Donor Era</b>		
(1998-2003)		
2004-2008	8.508	
2009-2012	73.705	0.000*
2013-2014	25.174	0.000*

Source: 1998-2014 Indiana Network for Patient Care

Notes: SCr24= Serum Creatinine laboratory follow-up data at 24-months

N = 1,212

a. Odds ratio =  $e^{\log\text{-odds}} = e^{\beta}$ . Also known as relative odds

b. P-values significant at <0.05 are marked \*

**Model # 7 UA24**

Variable	Odds Ratio <sup>a</sup> (OR)	P- value <sup>b</sup>
<b>Age</b>		
(19-39)		
40-49	0.504	0.118
50-59	0.743	0.500
60+	0.608	0.632
<b>Race</b>		
(Non-black or African-American)		
Black or African-American	2.080	0.115
<b>Donor Era</b>		
(1998-2003)		
2004-2014	2.293	0.088

Source: 1998-2014 Indiana Network for Patient Care

Notes: UA24= urinalysis laboratory follow-up data at 24-months

N = 1,212

a. Odds ratio =  $e^{\log\text{-odds}} = e^{\beta}$ . Also known as relative odds

b. P-values significant at <0.05 are marked \*

**Model # 8 UA24**

<b>Variable</b>	Odds Ratio <sup>a</sup> (OR)	<i>P</i> - value <sup>b</sup>
<b>Age</b>		
(19-39)		
40-49	0.515	0.129
50-59	0.756	0.526
60+	0.589	0.610
<b>Race</b>		
(Non-black or African-American)		
Black or African-American	2.101	0.110
<b>Donor Era</b>		
(1998-2004)		
2005-2014	2.578	0.35

Source: 1998-2014 Indiana Network for Patient Care

Notes: UA24= urinalysis laboratory follow-up data at 24-months

*N* = 1,212

a. Odds ratio =  $e^{\log\text{-odds}} = e^{\beta}$ . Also known as relative odds

b. *P*-values significant at <0.05 are marked \*

**Model #9 UA24**

<b>Variable</b>	Odds Ratio <sup>a</sup> (OR)	<i>P</i> - value <sup>b</sup>
<b>Age</b>		
(19-39)		
40-49	0.514	0.128
50-59	0.765	0.543
60+	0.543	0.557
<b>Race</b>		
(Non-black or African-American)		
Black or African-American	2.293	0.076
<b>Donor Era</b>		
(1998-2003)		
2004-2008	1.467	0.484
2009-2014	3.117	0.023*

Source: 1998-2014 Indiana Network for Patient Care

Notes: UA24= urinalysis laboratory follow-up data at 24-months

*N* = 1,212

a. Odds ratio =  $e^{\log\text{-odds}} = e^{\beta}$ . Also known as relative odds

b. *P*-values significant at <0.05 are marked \*

**Model #10 UA24**

<b>Variable</b>	<b>Odds Ratio<sup>a</sup> (OR)</b>	<b>P- value<sup>b</sup></b>
<b>Age</b>		
(19-39)		
40-49	0.518	0.134
50-59	0.768	0.549
60+	0.540	0.554
<b>Race</b>		
(Non-black or African-American)		
Black or African-American	2.278	0.078
<b>Donor Era</b>		
(1998-2004)		
2005-2008	1.716	0.304
2009-2014	3.293	0.011*

Source: 1998-2014 Indiana Network for Patient Care

Notes: UA24= urinalysis laboratory follow-up data at 24-months

N = 1,212

a. Odds ratio =  $e^{\log\text{-odds}} = e^{\beta}$ . Also known as relative odds

b. P-values significant at <0.05 are marked \*

**Note: Model # 11 of UA24 was selected for analysis and presentation in the manuscript**

**Model #12 UA24**

<b>Variable</b>	<b>Odds Ratio<sup>a</sup> (OR)</b>	<b>P- value<sup>b</sup></b>
<b>Age</b>		
(19-39)		
40-49	0.515	0.130
50-59	0.811	0.637
60+	0.600	0.625
<b>Race</b>		
(Non-black or African-American)		
Black or African-American	2.291	0.077
<b>Donor Era</b>		
(1998-2003)		
2004-2008	1.462	0.489
2009-2012	3.747	0.009*
2013-2014	1.104	0.907

Source: 1998-2014 Indiana Network for Patient Care

Notes: UA24= urinalysis laboratory follow-up data at 24-months

N = 1,212

a. Odds ratio =  $e^{\log\text{-odds}} = e^{\beta}$ . Also known as relative odds

b. P-values significant at <0.05 are marked \*



## Appendix C: Organ Procurement and Transplantation Network/United Network for Organ Sharing Living Donor Follow-Up Form Images

Records ?

Living Donor Follow-Up Worksheet

FORM APPROVED: O.M.B. NO. 0915-0157 Expiration Date: 02/28/2018

Note: These worksheets are provided to function as a guide to what data will be required in the online TIEDI® application. Currently in the worksheet, a red asterisk is displayed by fields that are required, independent of what other data may be provided. Based on data provided through the online TIEDI® application, additional fields that are dependent on responses provided in these required fields may become required as well. However, since those fields are not required in every case, they are not marked with a red asterisk.

Donor ID:

Provider Information

Recipient Center:

Followup Center:

Donor Information

Name:

DOB:

Transplant Date:

SSN:

Gender:

Donor ID:

Recovery Date:

Organ:

Donor Status

Date of Initial Discharge:

Date of last contact or death: \*

Most Recent Donor Status since: \*

Attempts to Collect: \*

Cause of Death:

Specify:

Functional Status:

Physical Capacity: \*

Working for Income: \*

If No, Not Working Due To:

If Yes:

☐ No Limitations
 ☐ Limited Mobility
 ☐ Wheelchair bound or more limited
 ☐ Unknown

☐ YES
 ☐ NO
 ☐ UNK

☐ Disability
 ☐ Insurance Conflict
 ☐ Inability to Find Work
 ☐ Donor Choice - Homemaker
 ☐ Donor Choice - Student Full Time/Part Time
 ☐ Donor Choice - Retired
 ☐ Donor Choice - Other
 ☐ Unknown

☐ Working Full Time
 ☐ Working Part Time due to Disability
 ☐ Working Part Time due to Insurance Conflict
 ☐ Working Part Time due to Inability to Find Full Time Work
 ☐ Working Part Time due to Donor Choice
 ☐ Working Part Time Reason Unknown
 ☐ Working, Part Time vs. Full Time Unknown

If Yes:	<input type="radio"/> Working Full Time <input type="radio"/> Working Part Time due to Disability <input type="radio"/> Working Part Time due to Insurance Conflict <input type="radio"/> Working Part Time due to Inability to Find Full Time Work <input type="radio"/> Working Part Time due to Donor Choice <input type="radio"/> Working Part Time Reason Unknown <input type="radio"/> Working, Part Time vs. Full Time Unknown
Loss of Insurance Due to Donation:	<input type="radio"/> YES <input type="radio"/> NO <input type="radio"/> UNK
If Yes:	<input type="checkbox"/> Loss of Health Insurance <input type="checkbox"/> Loss of Life Insurance

<b>Clinical Information</b>			
Current weight: *	Date: <input type="text"/>	<input type="text"/> lb <input type="text"/> kg	ST= <input type="text"/>
ER or urgent care visit related to donation since last follow-up: *			
<input type="radio"/> YES <input type="radio"/> NO <input type="radio"/> UNK			

<b>Kidney Clinical Information</b>			
Most Recent Values Since:			
Serum Creatinine:	Date: <input type="text"/>	<input type="text"/> mg/dl	ST= <input type="text"/>
Blood Pressure Systolic:	Date: <input type="text"/>	<input type="text"/> mm/Hg	ST= <input type="text"/>
Blood Pressure Diastolic:	Date: <input type="text"/>	<input type="text"/> mm/Hg	ST= <input type="text"/>
Donor Developed Hypertension Requiring Medication:	<input type="radio"/> YES <input type="radio"/> NO <input type="radio"/> UNK		
Urinalysis:			
Urine Protein:	<input type="radio"/> Positive <input type="radio"/> Negative <input type="radio"/> Not Done <input type="radio"/> Unknown		
or			
Protein-Creatinine Ratio:	<input type="text"/> GM/GM		
Maintenance Dialysis:	<input type="radio"/> YES <input type="radio"/> NO <input type="radio"/> UNK		
If Yes, Date First Dialyzed:	<input type="text"/>		
Diabetes:	<input type="radio"/> YES <input type="radio"/> NO <input type="radio"/> UNK		
Treatment:	<input type="checkbox"/> Insulin <input type="checkbox"/> Oral Hypoglycemic Agent <input type="checkbox"/> Diet		

<b>Lung Clinical Information</b>	
Activity Level:	<input type="radio"/> No change in activity level <input type="radio"/> Mild decrease in activity level <input type="radio"/> Moderate decrease in activity level <input type="radio"/> Severe decrease in activity level <input type="radio"/> Increase in activity level <input type="radio"/> Unknown
Chronic Incisional Pain:	<input type="radio"/> Mild <input type="radio"/> Moderate <input type="radio"/> Severe <input type="radio"/> Unknown
<b>Complications</b>	
Has the donor been readmitted since:	<input type="radio"/> YES <input type="radio"/> NO <input type="radio"/> UNK

**Kidney Complications since:**☐ YES ☐ NO ☐ UNK

If Yes:

☐ Added to UNOS TX candidate waiting list☐ Other, specify

Specify:

**Liver Complications since:**☐ YES ☐ NO ☐ UNK

If Yes:

☐ Bile Leak☐ Hepatic Resection☐ Abscess☐ Liver Failure☐ Added to UNOS TX candidate waiting list☐ Incisional hernia due to donation surgery☐ Other, specify

Specify:

**Complications since:**☐ YES ☐ NO

Specify:

**Recipient Information****Name:****Transplant Date:****SSN:**

## Appendix D: Literature Review of Studies of Living Donor Outcomes

Adapted from the Kidney Disease Improving Global Outcomes Evidence Review for the Development of Clinical Guidelines Michelle Brasure, PhD, MSPH, MLIS, Yelena Slinin, MD, MS, Maureen Carlyle, MPH, Areef Ishani, MD, MS, Keith Eidman, DO, Jason Bydash, DO, Saugar Maripuri, MD, MPH and Timothy J. Wilt, MD, MPH of the Minnesota Evidence Review Team: The Minneapolis VA Healthcare System and the Center for Chronic Disease Outcomes Research, the University of Minnesota Schools of Medicine and Public Health and Hennepin County Medical Center

### Living Kidney Donor Outcomes by Donor Age

#### *Renal function*

Ten studies reported renal function by age. In the three that looked at those with GFR  $<60 \text{ mL/min/1.73m}^2$ , all found older donors at greater risk (Dols et al., 2011; H. N. Ibrahim et al., 2009; J. H. Lee et al., 2007). Age at donation was significantly associated with greater odds of CKD (defined as  $\text{eGFR} <60 \text{ mL/min/1.73m}^2$ ) in three studies (H. N. Ibrahim et al., 2009; J. H. Lee et al., 2007; Lentine & Patel, 2012) and not associated in one study (Tsai et al., 2013). Greater donor age was correlated with lower GFR at follow-up in two studies in Swedish living donors (Fehrman-Ekholm et al., 2011; von Zur-Mühlen, Berglund, Yamamoto, & Wadström, 2014). Frequency of  $\text{eGFR} < 60 \text{ mL/min}$  was greater among donors who were 60 years or older at the time of donation compared to donors who were younger than 60 years of age (80% vs 31%) (Dols et al., 2011).

Older age at donation was associated with increased risk of CKD diagnoses as determined by administrative billing claims over an average 7.7 years follow-up (4% increase per year) (Lentine et al., 2010). Mean eGFR was 71ml/min/1.73m<sup>2</sup> among donors older than 60 at the time of donation compared to 78.5ml/min in younger donors after 6.7 years of follow-up (Gracida, Espinoza, Cedillo, & Cancino, 2003).

One study did not find any difference in eGFR, frequency of eGFR <60 ml/min/1.73m<sup>2</sup>, as well as eGFR < 45 ml/min/1.73m<sup>2</sup> among donors who donated before they turned 18 compared to donors who donated between the ages of 18 and 30 (MacDonald et al., 2014).

The one study that looked at serum creatinine found no difference at follow-up for those aged 21-35 and 36-50, but found a difference in those 51-69 (mean creatinine of 1.0 versus 0.8 mg/dL) (El-Agroudy et al., 2007). The quality of evidence for the outcome was deemed very low by KDIGO.

### *Hypertension*

Hypertension in LKDs was reported in six studies defined by either blood pressure or treatment by medication included in the KDIGO systematic review for the development of clinical practice guidelines. Dols et al. reported risk of HTN in older donors (>60 years old) comparable to that in younger donors (10% versus 6%, p=0.56) (Dols et al., 2011). In one study older age at follow-up was associated with 5 mmHg higher systolic blood pressure (Fehrman-Ekholm et al., 2011). Two studies reported that older age at donation

was associated with greater risk of drug treated hypertension (H. N. Ibrahim et al., 2009) (Lentine et al., 2014).

El-Agroudy et al. looked at hypertension medications in donors ages 21-35, 36-50 and 51-69 and reported a greater number of older donors using one or two medication than younger donors at 10.7 years of follow-up (12.6%, 32.5% and 31.8%) (El-Agroudy et al., 2007).

### *Diabetes*

One study reported that older age at donation was associated with a 5% higher risk of drug-treated diabetes over an average 7.7 years of follow-up (Lentine et al., 2010)

Lentine The quality of evidence for the outcome was deemed as low by KDIGO.

### *Living Donor Outcomes By Donor by Sex*

Seventeen studies analyzed donor outcomes by sex. The studies reported mean / median lengths of follow-up ranging from 5.4 to 12.2 years which is longer than the 24-month follow-up as presented in the present study. Quality of evidence was deemed to be low to very low for all of the outcomes by KDIGO.

### *Renal function*

Six studies reported renal function by gender. Two studies reported no significant increase in risk of post-donation eGFR <60 ml/min by MDRD in women compared to men (J. H. Lee et al., 2007; Tsai et al., 2013). One study reported greater odds of GFR <

60 ml/min/1.73m<sup>2</sup> in women compared with men (OR: 3.11; 95% CI:1.11 to 8.67) (H. N. Ibrahim et al., 2009). One study reported greater risk of claims for CKD in male donors compared to female donors (AHR: 1.64; 95% CI: 1.16 to 2.34) (K. L. Lentine et al.).

One study reported similar GFR in male (81.6) and female (79.4) donors at 10 year of follow-up, p-value was not (Karakayali, Moray, Demirag, Yildirim, & Bilgin, 1998) while another study reported higher MDRD eGFR in males (69+13 ml/min/1.73m<sup>2</sup>) than females (65+12 ml/min/m<sup>2</sup>), p<0.01.(von Zur-Muhlen et al.) The quality of evidence for the outcome was very low.

### *Hypertension*

Three studies reported HTN by gender (El-Agroudy et al.; K. L. Lentine et al., 2010; Tsai et al., 2013). In one study incidence of HTN was not different between male and female donors at 5.5 years (Tsai et al.). In another study HTN (>140/90 mmHg) was more common among female donors (24.7 versus 17.8%, p=0.03) (El-Agroudy et al., 2007). A third study revealed a greater risk of drug-treated HTN among male donors (AHR: 1.21; 95% CI: 1.03 to 1.43) (K. L. Lentine et al.). The quality of evidence for the outcome was very low.

### *Diabetes*

One study reported diabetes diagnosis by gender (K. L. Lentine et al.). There was no significant difference in risk of diabetes by claims diagnosis or drug-treated diabetes

between male and female donors (K. L. Lentine et al.). The quality of evidence for the outcome was very low.

### Living Donor Outcomes By Race

#### *Renal function*

One study compared eGFR in African American donors compared to African American non-donors. The average serum creatinine was  $1.2 \pm 0.3$  mg/dL and the average eGFR  $77 \pm 19$  mL/min/1.73 m<sup>2</sup> in donors and  $0.9 \pm 0.2$  mg/dL and  $109 \pm 17$  mL/min/1.73 m<sup>2</sup>, in non-donors, respectively at an average follow-up of 6.8 years. The number (proportion) of donors with an eGFR < 60 and < 45 mL/min/1.73 m<sup>2</sup> was 16 (15.5%) and 6 (6%), respectively, in donors while none of the non-donors had an eGFR < 60 mL/min/1.73 m<sup>2</sup> (Doshi et al., 2013). The quality of evidence for the outcome was low.

#### *Hypertension*

One study compared risk of hypertension defined as BP > 140/90 mmHg or use of blood pressure medications among African American donors and African American healthy non-donors. After a mean follow-up of 6.8 years, African American donors had greater risk of hypertension compared to African American non-donors (40.8% vs 17.9%, absolute difference of 22.9%, [RR: 2.3; 95% CI: 1.6 to 3.4]) (Doshi et al., 2013). The quality of evidence for the outcome was very low.



### *Diabetes*

One study compared risk of diabetes among African American donors and African American healthy non-donors. After a mean follow-up of 6.8 years, African American donors had a frequency of diabetes similar to that of African American non-donors (1.9% vs 1.7%, absolute risk difference of 0.2%, [RR: 1.14; 95% CI: 0.21 to 6.13]) (Doshi et al., 2013) The quality of evidence for the outcome was very low.

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## CURRICULUM VITAE

Macey L. Henderson

### EDUCATION

- PhD, 2016      Health Policy & Management, Indiana University Richard M  
Fairbanks School of Public Health at IUPUI, Indianapolis, IN  
PhD Minor: International Research Ethics  
Dissertation Title: *Living Kidney Donor Follow-up in a Statewide  
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- JD, 2011      Health Law and Bioethics, Indiana University Maurer School of  
Law, Bloomington, IN
- BA, 2008      Philosophy, Medical Humanities and Health Studies, Public  
Relations, Indiana University, Indianapolis, IN

### SPECIALTY EDUCATION AND TRAINING

- |           |   |   |
|-----------|---|---|
| 2012-2013 | Visiting Pre-Doctoral<br>Researcher               | Kennedy Institute of Ethics<br>Georgetown University              |
| 2012-2014 | Joint Bioethics Colloquium<br>Invited Participant | Department of Clinical Bioethics<br>National Institutes of Health |
| 2011      | Public Policy Mediation<br>Certificate            | School of Environmental and<br>Public Affairs                     |

		Indiana University
2010-2010	Transplant Management	Transplant Center
	Internship	University of Michigan
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	Internship	University of Michigan Health System

## **PROFESSIONAL APPOINTMENTS**

### *ACADEMIC*

2013-2016	Associate Instructor of	Indiana University Richard M
	Health Policy and	Fairbanks School of Public Health
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2014-2015	Research Coordinator	Purdue University School of
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2013-2014	Research Assistant	Regenstrief Institute, IU Center for
		Aging Research
2013	Coordinator	National Undergraduate Bioethics
		Conference Georgetown
		University
200-2008; 2012	Research Assistant	Department of Pediatrics, Section
		of Adolescent Medicine Indiana
		University School of Medicine

## *NON-ACADEMIC*

2014	Research Consultant	Mental Health of Greater Indianapolis
2013- Present	Series Editor	SpringerBriefs in Public Health Ethics Springer Publishing, Ltd
2013- Present	Research Consultant	Grand Slam III
2013	Evaluator	National Alliance for Mental Illness
2012	Educator	Science and Technology Fellowship Program National Academies of Science
2011-2015	Co-Founder & Research Consultant	Health Education, Research, and Outreach HERO Network, LLC

## **PROFESSIONAL ORGANIZATION MEMBERSHIPS**

2015 - Present	American Society of Transplantation	Trainee Member
2015 - Present	American Society of Transplant Surgeons	Trainee Member

2013-2014	Academy Health	Student Member
2013 – Present	Chicago Transplant Ethics Consortium	Member
2012 – Present	Network for Public Health Law	Member
2012 – Present	American Public Health Association	Member
2012 – 2013	National Kidney Foundation <i>Living Donor Council</i>	Member
2010 – Present	American Society for Bioethics and Humanities	Member

## PROFESSIONAL HONORS AND AWARDS

2015	Romanell Medical Education Fellowship	Academy for Professionalism in Healthcare
2012	40 Under 40 Nominee	Robert Wood Johnson Foundation
2011	Excellence in Legal Education, Law of Toxics and Hazardous Wastes	CALI Legal Institute
2010	Future of Fitness Feature	Oxygen Magazine

## RECENT PROFESSIONAL DEVELOPMENT

April 2016	Conference Participant	Academy for Professionalism in Health Care
May 2015	Conference Participant	Academy for Professionalism in Health Care
April 2015	Training Workshop Participant	Teaching Skills in International Research Ethics, NIH Fogarty Center
October 2014	Conference Participant	ASBH
June 2013	Intensive Bioethics Course	Kennedy Institute of Ethics
May 2013	Health Information Privacy	Indiana University School of Medicine

## PUBLICATIONS

### ***PEER REVIEWED***

1. Fisher, J.S., Butt, Z., Friedwald, J., Fry-Revere, S. Hannigan, J., **Henderson, M.L.**, Ladin, K., Mysel, H., Preczewski, L., Sherman, L., Theissen, C., Gordon, E.G. (2015). Between Scylla and Charybdis: Charting an Ethical Course for Research into Financial Incentives for Living Kidney Donation. *The American Journal of Transplantation*.



2. Nazir, A., Khan, B., Counsell, S., **Henderson, M.**, Gao, S. and Boustani, M. (2015), Impact of an inpatient geriatric consultative service on outcomes for cognitively impaired patients. *The Journal of Hospital Medicine*. doi: 10.1002/jhm.2326.
3. **Henderson, M.L.** & Chevinsky, J. (2014). Medical Ethics and the Media. The Value of a Story. *American Medical Association Journal of Ethics*: Volume 16, Number 8: 642-647.
4. **Henderson M. L.** Chevinsky, J., Biviji- Sharma, R., Mills, K. (2014). Improving Patient-Doctor Communication about Risk and Choice in Obstetrics and Gynecology through Medical Education: A Call for Action. *The Journal of Clinical Ethics*, Summer; 25(2):176.
5. Watson, D.P., Young, J., Ahonen, E.A., Xu, H., **Henderson, M.L.**, Shuman, V., Tolliver, R. (2014) Development and Testing of an Implementation Strategy for a Complex Housing Intervention: protocol for a mixed methods study. *Implementation Science*: 9:138.
6. Mullins-Owens, H.L., **Henderson, M.L.**, and Henderson, J. (2012). Protecting a vulnerable population with little regulatory framework: a comparative analysis of international guidelines for pediatric research ethics. *The Journal of Contemporary Health Law and Policy* 29, no. 1:36.
7. **Henderson, M.L.** (2012). Providing More Reasons for Individuals to Register as Organ Donors. *The Journal of Clinical Ethics* 23, no. 3:288.

## ***NON-REFEREED AND EVALUATION REPORTS***

1. **Henderson, M.L.** “Physician Autonomy in Health Advocacy for Friends and Family Members.” *The New England Journal of Medicine*.  
nejm.org, n.d. Web. 28, September 2014.
2. Ahonen, E.Q., **Henderson, M.L.**, and Day, K.M. (2014). The Implementation of the Aging Brain Care Program. Prepared for Centers for Medicaid and Medicare Service Innovation Grant.
3. **Henderson, M.L.**, and Greene, M.S. (2013). *Evaluation Protocol for the National Alliance on Mental Illness’ Connection Facilitator Training Program*. Prepared for the Indiana Chapter of the National Alliance for Mental Illness.
4. Arling, G., Abrahamson, K., Mueller, C., Davila, H., Black, A., **Henderson, M.L.**, Bennett, M., & Kouns, L. (2013). *Sustaining Quality Improvement in Long-Term Care: Findings from Minnesota’s Provider Initiated Performance Payments (PIPP) Initiative*. State of MN Department of Human Services.
5. **Henderson, M.L.** Organizational Ethics and Quality Improvement in Nursing Homes: Creating a Reflective Culture. *The Minnesota Connection Information Exchange*. State of MN. Department of Human Services. August 2, 2013.

## ***ETHICS CASES AND BLOGS***

1. **Henderson, ML** (2015) A Crucial Catch: The NFL, Ethics and Public Health Advocacy. *The American Journal of Bioethics Blog*.
2. **Henderson ML** and Doby, BL. (2015) A Matter of Ethics and Policy in Regenerative Transplantation in the United States. *The American Journal of Bioethics Blog*.
3. **Henderson, ML** (2015) Zion's Hands. Even NBC News Anchor Lester Holt is a Fan.
4. **Henderson ML** (2015) Financial Interventions and Living Organ Donation Research in a Learning Healthcare System. *The American Journal of Bioethics Blog*.
5. **Henderson ML** and Doby, BL. (2015): Planned Parenthood, Tissue Donation, and American Politics. *The American Journal of Bioethics Blog*.
6. **Henderson ML** (2015) Sofia Vergara, Nick Loeb, and a Bioethics Dilemma. *PopHealth*
7. **Henderson ML** and Chevinsky, J. (2015) The Oscars: Hollywood's Biggest Night and Why it Matters to Medicine and Public Health. *The American Journal of Bioethics Blog*.
8. **Henderson, M.L.** (2013). Evaluating Ethics Quality: What is IntegratedEthics?. *The Minnesota Connection Information Exchange*. State of MN Department of Human Services. August 9<sup>th</sup>.
9. **Henderson, M.L.** Making Tough Choices: Surrogate Decision Making in Long-Term Care. *The Minnesota Connection Information Exchange*. State

of MN Department of Human Services, August 30, 2013.

10. **Henderson, M.L.** (2013). Global Organ Transplant Tourism. National Undergraduate Bioethics Conference.
11. **Henderson, M.L.** (2013). Maternity Hotels. National Undergraduate Bioethics Conference.
12. **Henderson, M.L.** (2013). Allotransplantation, Essential Health Benefits, and the Patient Protection and Affordable Care Act. National Undergraduate Bioethics Conference.
13. **Henderson, M.L.** (2013). Geoengineering: Intentional Intervention to Mitigate Climate Change. National Undergraduate Bioethics Conference.

#### ***SPECIAL FEATURES AND POPULAR PRESS ARTICLES***

1. **Thompson, M.L.** Resolutions Done Right, Together. *The Huffington Post*, January 27, 2012.
2. **Thompson, M.L.** First Time Brides, Second Time Grooms. *The Huffington Post*, March, 18, 2012.
3. **Thompson, M.L.** “To Give Love”, February Feature, 60th Anniversary National Kidney Foundation Art Contest (2011).
4. “A Way to Give Life and Love” *The Bloomington Herald Times*. March, 2010.
5. “To Give Love” *The Indianapolis Star*. March, 2010.
6. “Macey Thompson-Future of Fitness Feature” *Oxygen Magazine*. June, 2010.

## PRESENTATIONS

### NATIONAL

1. Lee, L., Carrese, J, Gerber, P, Harter, P, **Henderson, ML**, Reynolds, PP., Sakhuja, M. (April, 2016). Integrating Ethics into Health Professions Education and Residency Training. The Academy for Professionalism in Health Care 4<sup>rd</sup> Annual Conference, Philadelphia, PA (4.5 hours)
2. **Henderson, ML**, Chevisnky, J., Ubel, P., Herron, P., Kuczewski, M. (October, 2015). *Connecting and Networking for Bioethics and Humanities Professionals*. The American Society for Bioethics and Humanities Annual Meeting, Houston, Tx.
3. Chevinsky, J., Herron, P., Kuczewski, M., **Henderson, M.L.** (May, 2015). *You Are What You Wear: Dress Code and the Modern Health Care Professional*. The Academy for Professionalism in Health Care 3<sup>rd</sup> Annual Conference, Louisville, KY.
4. **Henderson, M.L.** & Chevinsky, J. (May, 2015). *Developing an Interdisciplinary Medical Education Activity to Improve Professionalism in the Clinical Encounter about Risks, Preferences, and Values in Labor and Delivery Interventions*. The Academy for Professionalism in Health Care 3rd Annual Conference, Louisville, KY.
5. Paschall, B.D., Henderson, **M.L.**, Adams, N., Boustani, M. (November, 2014). *Reducing Health Disparities for Rural and Urban Communities via Tools of Implementation Science and an Innovative Academic Partnership Focused on Interprofessional Education*. American

Public Health Association Annual Meeting, New Orleans, LA.

6. Greene, M. & **Henderson, M.L.** (November, 2014). *Development of an Evaluation Protocol for the National Alliance for Mental Illness's (NAMI) Connection Facilitator Training Program*. American Public Health Association Annual Meeting, New Orleans, LA.
7. **Henderson, M.L.**, Chevinsky, J., Biviji-Sharma, R., Mills, K. (October, 2014). *Improving Doctor-Patient Communication about Risk, Choice, and Ethics in Obstetrics and Gynecology with Medical Education*. American Society for Bioethics and Humanities (ASBH) Annual Meeting, San Diego, CA.
8. Chevinsky, J., **Henderson, M.L.**, Herron, P., Kuczewski, M. (October, 2014). *Social Media Training Session for Bioethics and Humanities Educators-A Preconference Workshop*. ASBH Annual Meeting, San Diego, CA.
9. Chevinsky, J., **Henderson, M.L.**, Herron, P., Kuczewski, M. (October, 2014). *Twitter Workshop: A Guide for Inclusiveness in Bioethics and Medical Humanities*. ASBH Annual Meeting, San Diego, CA.
10. Chevinsky, J., **Henderson, M.L.**, Wysong, T.J. (July, 2014). *@BioethxChat: Utilizing Mass Media to Promote Student, Professional, and Public Engagement in Bioethics and Humanities*. Yale University Summer Bioethics Institute, New Haven, CT.
11. Abrahamson, K., Mueller, C., Davila, H., **Henderson, M.L.**, Kouns, L., Arling, G.A. (July, 2014). *Making Changes Stick: Sustainability of*

*State-Sponsored Nursing Home Quality Improvement Projects.*

Academy Health Annual Research Meeting, San Diego, CA.

12. **Henderson, M.L.**, Adams, N., Norwood, C.W., Boustani, M. (May, 2014). *Preparing the Public Health Workforce with the Tools of Implementation Science.* American Association of Medical Colleges (AAMC) Annual Health Workforce Conference. Washington, D.C.
13. **Henderson, M.L.**, LaValley, D., Savel, T. (May, 2014). *Applications of New Technologies for Public Health Solutions.* Centers for Disease Control Prevention (CDC) and the National Association of County and City Health Officials (NACCHO) Public Health Informatics Conference, Atlanta, GA.
14. **Henderson, M.L.**, Taylor, C., Barnett, R. (November, 2013). *OBGYN Clerkship in Undergraduate Medical Education: Ethical Issues and Informed Consent.* American Medical Association Interim Meeting and Conference, National Harbor, MD.
15. **Henderson, M.L.**, Veatch, R.M. (November, 2012). *Over My Dead Body: Incentivizing Organ Donation.* Georgetown University, National Bioethics Reference Center, Washington, D.C.
16. **Henderson, M.L.**, Veatch, R.M. (October, 2012). *Theories of Distributive Justice and Scarce Resource Allocation.* Georgetown University, Department of Philosophy, Washington, D.C.

## REGIONAL

1. **Henderson, M.L.** (August, 2010). *Results of a Needs Assessment on the Development of a Hospital Transplant-specific Ethics Committee.* University of Michigan Transplant Center.
2. **Henderson, M.L.**, and Kamil, L.K. (June, 2010). *Healthcare Provider Legal Liability and Providing Testimony.* Eastern Michigan University, School of Health Sciences, Ypsilanti, MI.
3. **Henderson, M.L.** and Kamil, L.K. (May, 2010). *Understanding HIPAA: Compliance for Allied Health Professionals.* Eastern Michigan University, School of Health Sciences, Ypsilanti, MI.

## LOCAL

1. **Henderson, M.L.**, Mullen, C., Comer, A.M., Church, A.K., Osburn, L.L., Stone, C.L. (April 2014). Improving Public Health Action in Transit Legislation. Robert G. Brindle Civic and Community Engagement Symposium.
2. **Henderson, M.L.**, Mullen, C., Comer, A.M., Church, A.K., Osburn, L.L., Stone, C.L. (April 2014). *A Student Collaboration to Promote Transit Legislation.* Central Indiana Urban Health Conference.
3. **Henderson, M.L.** (February, 2013). *Reflections on the Body: Living Organ Donation.* Seminars in Medical Humanities and Health Studies at IUPUI, Indianapolis, IN.
4. **Henderson, M.L.** (June, 2012). *The Conceptualization of Community in International Research in Pediatrics.* Department of Pediatrics, Indiana



University School of Medicine.

5. Mirchandani, A.M., **Henderson, M.L.**, Mullins-Owens, H.L., Henderson, J. (March 2012). *Attitudes and Perceptions of Living Kidney Donor Evaluation*. IUPUI Research Day.
6. **Henderson, M.L.** (April, 2011). *Compensation for Families Consenting to Research Autopsy for Children in a Study of Malaria Mortality in West Africa*. Indiana University Center for Bioethics.
7. **Henderson, M.L.**, (April, 2011). *The Law of Organ Procurement and Transplantation*. Indiana University Maurer School of Law, Bloomington, IN.
8. **Henderson, M.L.** (February, 2011). *The Challenge of Informed Consent in International Research: Epidemiology in West Africa*. Indiana University Center for Bioethics.
9. **Henderson, M.L.** (February, 2011). *Alternative Careers in Health Law: Bioethics and Public Health*. Indiana University Maurer School of Law, Bloomington, IN.
10. **Henderson, M.L.** (February, 2010). *Staying Healthy in Law School: Health and Wellness for Professional Students*. Indiana University Maurer School of Law, Bloomington, IN.
11. **Henderson, M.L.** (October, 2010). *Organ Procurement Systems: Ethical and Practical Solutions for Increasing the Available Supply of Organs for Transplant*. Indiana University Maurer School of Law,

Bloomington, IN.

12. **Henderson, M.L.** (October, 2009). *Ethical Issues Associated with Organ Procurement Organizations*. Indiana University School of Medicine, Indianapolis, IN.

## TEACHING

<i>Course</i>	<i>Title</i>	<i>Term</i>	<i>Type</i>	<i>Enrollment</i>
H474	Healthcare Administration Ethics Community and Public Health Ethics	Spring 2016	Seminar, didactic	48
H474	Healthcare Administration Ethics Community and Public Health Ethics	Fall 2015	Seminar, web-based	47
H501	US Healthcare Systems and Health Policy	Summer 2015	Web-based	6

H474	Healthcare Administration Ethics Seminar	Spring 2015	Seminar, didactic	13
P300	Public Health Ethics	Spring 2015	Seminar, didactic	13
H474	Healthcare Administration Ethics Seminar	Fall 2014	Seminar, didactic	32
H501	US Healthcare Systems and Health Policy (TA)	Summer 2014	Web-based	5
H474	Healthcare Administration Ethics Seminar	Spring 2014	Seminar, didactic	17
H474	Healthcare Administration Ethics Seminar (TA)	Fall 2013	Seminar, didactic	46
H624	Developing Strategic Capability (TA)	Fall 2014	Didactic	30

## **PAST RESEARCH ACTIVITY AND SUPPORT**

Research Coordinator, Greg Arling, PhD Principal Investigator, “*Study of a State-Level Model for Transitioning Nursing Home Residents to the Community*”, Agency for Healthcare Quality and Research R-18, \$479,000, 2014-2015.

Conference Coordinator, Greg Arling, PhD Principal Investigator, “*Incentivizing Better Quality in Long-Term Care: Where Do We Stand and Where Do We Go From Here?*” Agency for Healthcare Quality and Research R-13, \$35,000, 2014-2015.

Investigator, Malaz Boustani, MD, MPH Principal Investigator, “*Dissemination and Implementation of the Aging Brain Care (ABC) Medical Home*”, Centers for Medicare and Medicaid Innovation Center, \$7,600,000, 2014-2015.

Research Assistant, Greg Arling, PhD Principal Investigator, “*Evaluating a Comprehensive State-Model to Improve Nursing Home Quality*”, Agency for Healthcare Research and Quality, \$479,000, 2013-2014.

Research Assistant, Greg Sachs, MD Principal Investigator, “*Optimizing Patient Transfers, Impacting Medical Quality, and Improving Symptoms: Transforming Institutional Care: The OPTIMISTIC Project*”, Centers for Medicare and Medicaid Innovation Center, \$13,000,000, 2013-2013.

Investigator, Matthew Aalsma, PhD Principal Investigator, “*Indianapolis Teenage Education for Pregnancy Prevention*”, Nina Mason Pullian Charitable Trust, \$45,000, 2012-2012.

Research Assistant, Kathleen Hanna, PhD, RN Principal Investigator, “*The*

*Transition to Young Adulthood among Late Adolescents with Type 1 Diabetes*”,  
National Institutes of Health-National Institute of Nursing Research, \$401,840,  
2008-2008.

Research Assistant, Dennis Fortenberry, MD, MS Principal Investigator,  
“*Sexually Transmitted Infection Developmental Epidemiology of Young  
Women*”, National Institute of Allergies and Infectious Diseases, \$95,903, 2006-  
2008

## **SERVICE**

### *UNIVERSITY*

Public Health Corps, Member, 2013 – 2014

MPH Internship, Preceptor, 2012 – 2013

Philosophy Club, Member, 2007 – 2008

PhD Student Association, Officer, 2013 -2014

Indiana Public Health Week, Volunteer, 2014

Careers in Public Health Day, Volunteer, 2013

Health Law Society, Board Member, 2008 – 2011

Careers in Medical Humanities, Panelist, 2013

### *LOCAL*

Crooked Creek Community Center, Board Member, 2013 – 2014

## *REGIONAL*

United Network for Organ Sharing, Region 10 Member, 2010 – 2014

## *NATIONAL*

U.S. Organ Procurement and Transplantation Network (OPTN)

Workgroup on Imminent Death Donation, Member, 2014 – Present

OPTN/UNOS Living Donor Committee, Member (At-Large), 2014 – Present

OPTN/UNOS Living Donor Data Subcommittee, Member, 2014 – Present

OPTN/UNOS Living Donor Evaluation Subcommittee, Member,  
2014 – Present

American Society for Humanities and Bioethics, Social Media Task Force,  
2013 – Present

American Society of Transplantation, Live Donor Community of Practice,  
2012 – 2013

National Kidney Foundation, Living Donor Council, 2011 – 2013

## *AD HOC EDITORIAL ACTIVITY*

American Journal of Obstetrics and Gynecology

Annals of Internal Medicine

Pedagogy in Health Education Journal, Society for Public Health Education

American Public Health Association, *Ethics SPIG and Law abstract reviewer*

American Journal of Public Health

Journal of Internet Medical Research

Indiana Continuing Legal Education, Sports Law Seminar

## **PATIENT CARE & RELEVANT CLINICAL EXPERIENCE**

Practicum in Ethics, Indiana University (IU) Health, Fairbanks Center for Medical Ethics, 2011

Pediatric Ethics Committee, University of Michigan Health System, Summer 2010

Critical Care Extender Intern, David Geffen School of Medicine at UCLA, 2004

Assistant to the Director, Student Health Services, Pepperdine University, 2003

Neonatal Intensive Care Unit Volunteer, IU Health, Riley Hospital for Children, 2003

## **MEDIA, ENTERTAINMENT AND DIGITAL PRODUCTION EXPERIENCE**

2015	WXIN (FOX, Indianapolis)	Guest Executive Producer with Nicole Pence <i>#GotHeart Campaign Raises Organ Donor Awareness</i>
2015	WTHR (NBC Indianapolis)	Guest Executive Producer with Naomi Pescovitz <i>Carmel Couple Celebrates Gift of Life this Valentine's Day</i>

2015	WOOD TV8 (NBC West Michigan)	Consulting Producer with Marc Thompson <i>National Organ Donor Day</i>
2015	KDVR Fox 31 (Denver)	Production Shadow with Emmy award winning <i>Colorado Everyday</i>
2011	National Kidney Foundation	60 <sup>th</sup> Anniversary Calendar <i>February: To Give Love</i>
2009	WOOD TV 8 (Grand Rapids, Michigan)	News Research
2008 – 2011	“Macey Leigh LLC”	CEO and Creator
2007 – 2008	“Playing for Keeps EPSN950	Associate Producer
2004 – 2006	Pathway Productions, LLC	Digital Production Intern
2001 – 2003	Visionary Productions/Grand Slam	Production Associate
1999 – 2001	Hendu Entertainment	Production Assistant